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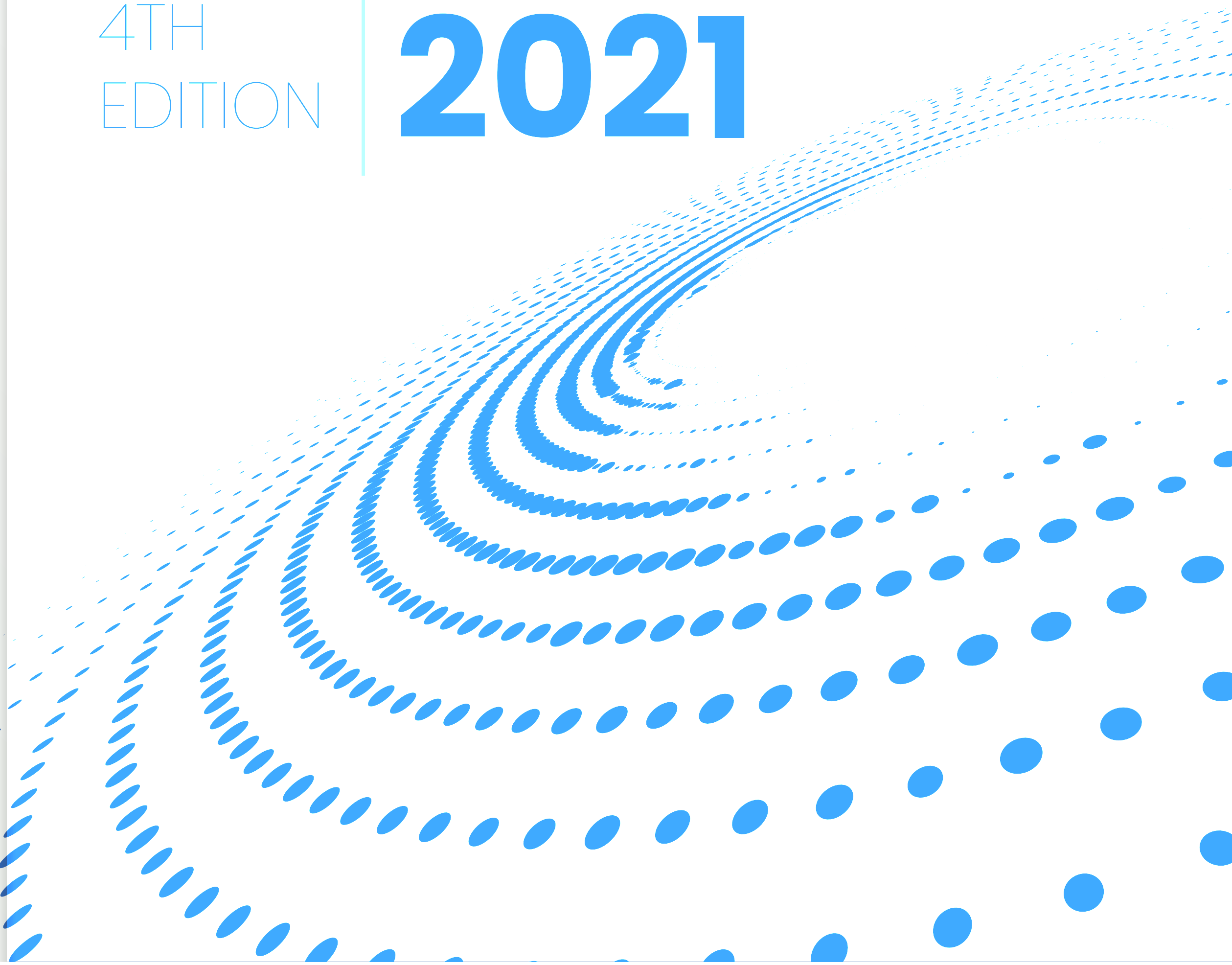
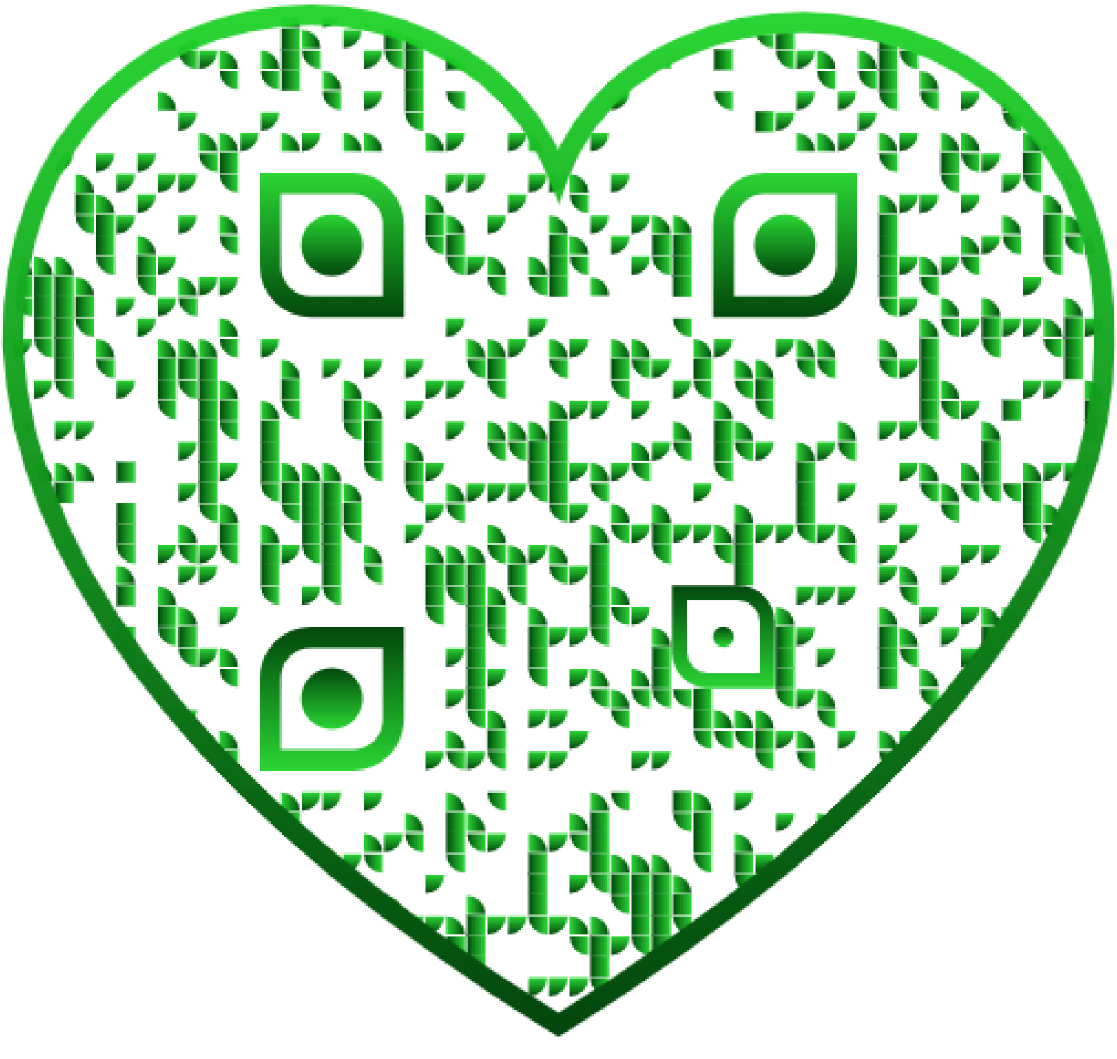
MINISTRY OF HEALTH-ETHIOPIA

STANDARD TREATMENT GUIDLINES FOR GENERAL HOSPITAL

4TH
EDITION

2021





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The leadership from AMR prevention and containment coordinating team at the Ministry of health to coordinate and support the development of this guideline is also acknowledged.

Sincere appreciation is also extended to the members of the core, technical and editorial team for their unreserved effort to bring this document to reality.

Lastly, but not least, the Ministry would also like to recognize and acknowledge the contributions of all individuals and organizations (Annexed) who participated and contributed in the revision processes.

ACRONYMS

ACD	Allergic contact dermatitis
ACEIs	Angiotensin converting enzyme inhibitors
ACS	Acute Coronary Syndrome
ADL	Acute adenolymphangitis
ADRs	Adverse Drug Reactions
AFB	Acid fast Bacilli
AIVR	Accelerated Idioventricular Rhythm
AKI	Acute kidney Injury
ALF	Acute liver failure
ARBs	Angiotensin receptor blockers
ART	anti-retroviral therapy
AV	Atrio ventricular
AWaRe	Access, Watch, Reserve
BMI	body mass index
C/Is	Contraindications
CBC	Complete blood count
CDAD	Clostridium Difficille Associated Disease
CKD	Chronic kidney Injury
CL	Cutaneous leishmaniasis
CLL	Chronic lymphocytic leukemia
CML	Chronic Myelogenous Leukemia
CNS	Central nervous system
COPD	Chronic Obstructive Pulmonary Disease
CPR	Cardiopulmonary resuscitation
CRP	C-reactive protein
CSF	Cerebrospinal fluid
D/Is	Drug interactions
D/S	Dextrose in Saline solution
D/W	Dextrose in water solution
DBS	Dry Blood Spot
DEC	Diethylcarbamazine citrate
DKA	Diabetic Ketoacidosis
DLA	Dermatolymphangioadenitis
DMARD	Disease-modifying anti-rheumatic medicines
DST	Medicine Susceptibility Testing deep vein thrombosis
DVT	deep venous thrombosis

ECG	electrocardiogram
ENL	Erythema Nodosum Leprosum
ENT	Ear, Nose and Throat
ESR	Erythrocyte sedimentation rate
ESRD	End Stage Renal Disease
FH	Fulminant hepatitis
FPG	Fasting plasma glucose
GDM	Gestational Diabetes Mellitus
GERD	Gastro Esophageal Reflux Disease
GFR	Glomerular Filtration rate
GI	Gastrointestinal
GTD	Gestational Trophoblastic diseases
GTN	Gestational Trophoblastic Neoplasia
HDL	High-density lipoprotein cholesterol
HHS	Hyperosmolar Hyperglycemic State
Hrs	Hours
ICD	Irritant Contact Dermatitis
IDU	Intravenous medicine use
IHCP	Intra-hepatic cholestasis pregnancy
IM	Intramuscular
IMU	Intravenous Medicine Use
IOP	Intra-ocular pressure
IRIS	Immune Reconstitution Immune Syndrome
ITP	Immune Thrombocytopenic Purpura
IU	International Unit
IUGR	Intrauterine growth restriction
IV	Intravenous
IVDA	Intravenous medicine abuse endocarditic
LDL	Low-density lipoprotein cholesterol
MAT	Multifocal Atrial Tachycardia
MDR	Multi Drug Resistance
MDT	Multi- Drug therapy
mL	Milliliter
MNT	Medical Nutrition Therapy
MOH	Ministry of Health of Ethiopia
MSH	Management Sciences for Health
N/S	Normal saline solution
NNRTI	Nucleoside Reverse Transcriptase Inhibitors
NNRTIs	Non-Nucleoside Reverse Transcriptase Inhibitors

NSVT	Non sustained ventricular tachycardia
NVE	native valve endocarditic
OGTT	Oral Glucose Tolerance Test
P.O	Per Os (mouth)
P/Cs	Precautions
PCP:	Pneumocystis Carinni Pneumonia
PEP	Post-exposure prophylaxis
PIs	Protease Inhibitors
PKDL	Post kala-azar Dermal Leishmaniasis
PMTCT	Prevention of mother-to-child transmission
PPH	Post-Partum Hemorrhage
PrEP	Pre-exposure prophylaxis
PRN	As required
PROM	Premature Rupture of Membranes
PSVT	Paroxysmal supra-ventricular tachycardia
PTE	Pulmonary thrombo-embolism
PTT	Placental trophoblastic tumor
PVE	Prosthetic Valve Endocarditis
RA	Rheumatoid Arthritis
RBC	Red blood cells
RDT	Rapid Diagnostic Tests
RUTF	Ready to use therapeutic feeding
SBMG	Self-blood glucose monitoring
SBP	Prophylaxis for spontaneous bacterial peritonitis
SSIs	Surgical site infections
STG	Standard Treatment Guideline
STI	Sexually transmitted infections
TID	Three times a day
VT	Ventricular Tachycardia
VTE	Venous thromboembolism
WBC	White blood cell count
WPW	Wolff-Parkinson-White

FORWARD

The Ethiopian Standard Treatment Guideline (STG) was first published in 2004 which is recognized as the first edition. There were subsequent revisions then after. The current edition is the fourth one. The reasons behind the revision of the STG are the dynamic nature of medicine, change in diagnostic and therapeutic modalities, updates in health strategies and policies as well as the advancement in Technology.

The current edition of the STG has 23 chapters. Four new chapters are added which was not partially or completely addressed by the previous editions. These four chapters include antimicrobial resistance and its containment, Care of patients in Ambulatory and Hospitalized settings, Oral and dental conditions, and Palliative care.

The antimicrobial resistance and its containment chapter is designed to address the alarmingly increasing burden of antimicrobial resistance. It is enriched with national data revealing the higher prevalence of antimicrobial resistance. The chapter is designed to introduce the WHO AWaRe strategy of saving antimicrobial agents which are aligned with the Ethiopian Essential Medicines List. The Ethiopian antimicrobial stewardship guideline is considered and incorporated.

The care delivered to patients at the out-patient or hospitalized setting is not well structured in Ethiopia. Such care ultimately has an impact on the quality of care delivered and treatment outcome. The current edition of the STG addressed this new concept clearly and understandably to the Ethiopian health workforce.

Dental and Oral Health in Ethiopia is at its infancy stage of integration to the other services. It has been considered as a separate disciple and health care delivery settings were delivered separately though patient needs are not designed in such a way. The current STG incorporated this new concept to ensure continuity of service and better health care delivery. As we move forward through evidence-based medicine with the support of science and technology; early diagnosis and early treatment will improve survival. Early diagnosis might bring non-curable health conditions as well as treatment-related survival will bring new health related conditions which cannot be avoided completely. Ultimately the quality of life will be compromised with pain, hypoxia, insomnia, mental conditions, and other health needs that palliative care can bring a difference. Through palliative care and the disciplines around, care and treatment services will be complete. The current guideline included a chapter on palliative care with is aligned with the national palliative care guideline as well as context.

The STG preparation process is well documented as a separate chapter to reveal the due process that the revision process went though. Trust and credibility will be ensured as the users of the guideline are plenty much behind. The current fourth edition of STG is designed to be user-friendly that health care workers (physicians, nurses, and pharmacists) can utilize in their work discipline to provide comprehensive care to their patients. The guideline is also aligned with other program-related guidelines as well as clinical management guidelines in the country. Users of the guideline are also forward their practical challenges to be included in the STG and were done accordingly.

Several stakeholders from different health-related disciplines (Policy makers, health leaders, program leads, clinicians, health educators, professional societies, support staffs and partners) are engaged in the due process of the preparation of the guideline. Several sessions of consultation and discussion forums were conducted. Ideas, opinions, challenges, opportunities, threats, possible solutions were forwarded. There is no conflict of interest.

The Federal Ministry of health and agencies in it (EFDA, EPSA, Ethiopian Health Insurance agency) are working to consider the STG as a binding document for health service delivery in Ethiopia. Patients will receive at least the minimum care at the STG. The STG will help to secure the drugs and supplies in the health facilities to implement it which ultimately improve health care delivery. Proper implementation of the STG will induce accountability as well as trust to the health facilities. It will help to implement health care financing, data quality, task sharing and shifting as well as many more components of the WHO building blocks in health care. Periodic monitoring and evaluation of STG implementation is mandatory for further enrichment as health care is a dynamic process and change is always imminent. Further revision should be based on the outputs of the monitoring and evaluation data.

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THE STG REVISION PROCESS

The availability of multiple treatment options will put a great pressure on the healthcare practitioners and increase healthcare costs and compromise the quality of care. The development, on time revision and implementation of standard treatment guidelines (STGs) thus is a crucial strategy for prioritizing and tailoring care to the local context, ensuring effective and safe use of medicines, containing health care costs, and preventing antimicrobial resistance.

By providing specific and clear recommendations for each clinical condition management, STGs promote an effective and economic use of medicines at different levels of health facilities. Therefore, a given treatment guidelines should provide up-to-date information relevant to the prevention, diagnosis and treatment of common health care problems in Ethiopia for the provision of quality care to patients.

Based on this understanding the guideline was revised with the consideration of the following basic components:

i) **The disease/conditions to be covered** to the Ethiopian context.

ii) **Guideline category and level of application:** health center, primary hospital and general hospital level as per the Ethiopian healthcare system and pharmaceutical delivery context.

iii) **Intended users of the guideline:** the physicians, health officers, nurses, clinical pharmacists, and other allied health personals.

iv) **Guideline objective(s):** focus on the inclusion of specific and tailored recommendations to the particular level of the health care system.

v) **Interventions and practice considerations**: the following key practice areas were specifically considered as a guiding scope of the revision process for every healthcare problem to be addressed:

Topic	
Brief description	• Definition or simple description and/or classification and/or epidemiology and/or causes and/or risk factors • Present based on relevance • Incorporating local epidemiologic data (if available EDHS, meta-analysis, national level (large scale) studies, Ethiopian WHO reports etc…are preferred) • Tailoring (for broader topics) to the points that will be addressed in the consecutive diagnosis and treatment is required.
Clinical features:	• Symptoms and/or • Signs
Investigations and diagnosis	• Most appropriate and practical investigations • Diagrammatic illustrations if likely (if possible, extend to include treatments for each algorithm point) • Not to miss popular/confirmatory methods
Treatment	• Goals of treatment • Pharmacologic (most appropriate and practical once) o Not to miss specific dose and administration points o Not to miss discussing clinically significant side effects and their management o Will be good if special population considerations forwarded o Based on AWaRe classification (only for antibiotics) and indicate stewardship considerations as necessary (for infectious cases) o Non pharmacologic (most appropriate and practical once)
	• Additional considerations,
	o Special population considerations o Perioperative considerations
Prevention	• As necessary • Relevant and/or most-up-to-date once • Focus on local studies and resource • Please do not hesitate to included important points if no reference

The STG The revision process passed through the following steps:

- Appointing a consultant by USAID MTaPS program
- Establishing of STG technical working group by MOH
- Establishing of STG steering committee by MOH,
- kickoff and successive supportive meetings among the MOH, MTaPS and consultants
- Preparing zero draft list by consultants
- Participating in the EEML consultative meetings and aligning with the EEML
- Refining and submitting the first draft to MTaPS and MOH
- Reviewing of final STG by specialists, experts and service delivery units. Subject area experts from specialized centers across all corners of the country underwent a 16 days extensive review of the document. The central core team selected by MOH with the consultants facilitated the review process, collect comments forwarded and revise the document.
- Finalization of the document and editorial work will be undertaken to produce a print ready form for approval by the MoH leadership.

The STG was revised based on evidence-based approach with efforts of contextualization to the local contexts. Accordingly, four new chapters were added upon consultant suggestion and consensus to increase the total chapters from 19 to 21 in the current version. In addition, new addition, deletion, or change/modifications was made to the previous editions.

The following four new chapters were included based on the current health care demand and associated national strategic directions. Except the basics of AMR have been presented under the first chapter of the previous revision, the rest three new chapters were not considered in the previous revision.

1) Antimicrobial al resistance and containment (Included as Chapter 2 in the revised content): The inclusion of containment strategies tailored to the health system level may help the overall containment effort of the country and is in line with the current global demand.

2) Care of patients in ambulatory and hospitalized setting (Included as Chapter 3 in the revised content): Despite the routine care issues are always there, it is largely overlooked in terms of having shared modeling and provision of consistent standard and safe care.

3) Oral and dental conditions (Included as Chapter 20 in the revised content): Given the high demand of dental care and the expansion of dental clinics in the country, it is indispensable to include in the current revision.

4) Palliative care (Included as Chapter 23 in the revised content):The MOH had developed a national palliative guideline (2016) to address increasing demand for the inclusion of the service to the Ethiopian healthcare system and to meet the needs of people suffering from cancer and other non-communicable conditions that require this specialized care. In line to this we included it to acknowledge the demand.

Although major changes were made across all chapters, some topics were almost completely rewritten as in the case of the pediatric disorders. Multiple new topics were introduced under the Emergency conditions and neurologic disorders too.The modifications made can be stated in to the following three themes 1) Introducing new topics (across almost all chapters), 2) removing topics (done extremely rarely) and 3) moving topics form one chapter to the other mainly based on consensus.

Despite different relevant and up-to-date scientific evidence were cited as indicated in each specific section, the following national materials have been used as a source document while revising the STG.

- Ethiopian Essential Medicine List (EEML-2020); Ministry of Health/ Ethiopian Food and Drug Administration, Addis Ababa, September 2020.
- Guideline for Diagnosis, Treatment and Prevention of Leishmaniasis in Ethiopia, 2nd edition (June, 2013)
- National Comprehensive Guidelines for Clinical and Programmatic Management of Major Non-Communicable Diseases (February, 2016)
- National palliative care Guideline, 2016
- National consolidated Guideline for comprehensive HIV prevention, care and treatment (August, 2018)

- National Essential Medicine List (5th edition, 2020)
- National guideline for prevention and control of viral hepatitis (2016-2020)
- National guideline for TB, DR-TB and Leprosy in Ethiopia, 6th edition (August, 2018)
- National Malaria Guideline (March, 2018)
- National viral hepatitis management guideline for Hepatitis C Virus (November, 2019)
- Standard Treatment Guidelines for General Hospitals, 3rd ed. Food, Medicine and Health Care Administration and Control Authority, Addis Ababa, 2014

The support from FMOH and MSH, consultants working at academic institution with different networks, different expert forums, and availability of program related diseases guidelines (HIV, TB, Malaria, STI etc.) were the opportunities for the STG development. Coronavirus (COVID-19) pandemic, internet interruption (in the month of July) and shortcomings for wider expert engagement were some of the limitations in the revision process.

To this end, we want to highlight that this latest version of the STG will have paramount worth to support the medical practice. Hence, shall be widely accessible in both electronic and printed forms.

Note: The information presented in these guidelines conforms to the current medical, nursing and pharmaceutical practice. Contributors and editors cannot be held responsible for errors, individual responses to medicines and other consequences.

CHAPTER I:

GOOD PRESCRIBING AND DISPENSING PRACTICES

Prescription is the link between the prescriber, the pharmacist (or dispenser) and the patient. It is important for the successful management of the presenting medical condition. Prescribers fill the diagnosis or ICD code for proper communication with the dispenser and choice of the medicine among the available generic options. Readers are kindly requested to refer "Ethiopian Medicines Good Prescribing Practices (GPP)" and Medicines Good Dispensing Practice guideline/manual.

Rational use of medicines is a mechanism through which safe, effective and economic medication is provided. It is promoted through the collaborative efforts of prescribers, dispensers, patient and policymakers. Rational prescribing ensures adherence to treatment and protects medicine consumers from unnecessary adverse medicine reactions. The prescriber could be a physician, a nurse or health officer or any health professional authorized to prescribe. Rational dispensing, on the other hand, promotes the safe, effective and economic use of medicines. The dispenser could be a pharmacist, and pharmacy technician. Prior to prescribing or dispensing any medicines, the prescriber or dispenser should make sure that it is within his/her scope of practice.

Medicines should only be prescribed when necessary, and the benefit-risk ratio of administering the medicine should always be considered prior to prescribing. Irrational prescribing leads to ineffective, unsafe and uneconomical treatment. Thus, it is very important that steps are taken to promote rational medicine use in order to effectively promote the health of the public especially given limited resources. One way of promoting rational medicine use is through the development and use of standard treatment guidelines.

Rational approaches to therapeutics require careful evaluation of health problems and selecting appropriate therapeutic strategies. Making the right diagnosis is the cornerstone for choosing the right kinds of therapy. Based on the diagnosis, health workers may select more than one treatment and the patient should agree with the selected treatment. The treatment could be pharmacologic or non-pharmacologic. It is important to consider the total cost of treatment in the selection process. The process should also consider efficacy, safety, suitability and availability. Medicine treatment should be individualized to the needs of each patient as much as possible. The concept of good clinical practice has to be incorporated within rational prescribing.

A major step towards rational use of medicines was taken in 1977, when WHO established the first Model List of Essential Medicines to assist countries in formulating their own national lists. Essential medicines are those that satisfy the priority health care needs of the population. Using an essential medicine list (EML) makes medicine management easy; and prescribing and dispensing are easier for professionals if they have to know about fewer essential items. This current standard treatment guideline is used as a resource to prepare the updated national EML of the country. EML should be regularly updated to consider the changes in need of the public at different time. Public sector procurement and distribution of medicines should be limited primarily to those medicines on the EML, and it must be ensured that only those health workers approved to use certain medicines are supplied with them. Healthcare professionals are recommended to refer the annexed EML for Ethiopia for further.

PRESCRIPTION WRITING

A prescription is electronic or paper based therapeutic transaction between the prescriber and dispenser. It is a written order by the prescriber to the dispenser on how the medicine should be dispensed. It serves as a means of communication among the prescriber, dispenser and medicine consumer, pertaining to treatment or prophylaxis.

A prescription should be written on a blank standard prescription legibly and clearly in ink and using generic names of the medicine(s). Some facilities may use electronic system.

A prescription should contain **(Annex)**

- Name, address, age, body weight of the medicine consumer and date of the prescription;
- Diagnosis; Generic name, dosage form and strength and directions for use of the medicines. The pharmaceutical form (for example 'tablet', 'oral solution', 'eye ointment', 'cream') should also be stated.

- The strength of the drug should be stated in standard units using abbreviations that are consistent with the Systéme Internationale (SI). 'Microgram' and 'nanogram' should not, however, be abbreviated. Also, 'units' should not be abbreviated. Avoid decimals whenever possible. If unavoidable, a zero should be written in front of the decimal point.
- Prescriber's name, signature and address.

Directions specifying the route, dose and frequency should be clear and explicit; use of phrases such as 'take as directed' or 'take as before' should be avoided. For preparations which are to be taken on an 'as required' basis, the minimum dose interval should be stated together with, where relevant, the maximum daily dose. It is good practice to qualify such prescriptions with the purpose of the medication (for example 'every 6 hours as required for pain', 'at night as required sleeping'). It is good practice to explain the directions to the patient; these directions will then be reinforced by the label on the medicinal product and possibly by appropriate counseling by the dispenser. It may be worthwhile giving a written note for complicated regimens although it must be born in mind that the patient may lose the separate note.

GOOD DISPENSING PRACTICE

Good Dispensing Practices ensure that the correct medicine is delivered to the right patient, in the required dosage and quantities, with clear information, and in package that maintains an acceptable potency and quality of the medicine. Dispensing includes all the activities that occur between the times the prescription or oral request of the patient or care provider is presented and the medicine is issued.This process may take place in health institutions or community drug retail outlets. It is often carried out by pharmacy professionals. No matter where dispensing takes place or who does it, any error or failure in the dispensing process can seriously affect the care of the patient mainly with health and economic consequences. Therefore, the dispenser plays a crucial role in the therapeutic process. The quality of dispensing may be determined by the training and supervision the dispenser has received. During medicines dispensing and counseling the information mentioned under prescribing above, the "Medicines Good Dispensing Practices" manual 2012 edition. Finally, an application of the professional code of ethics by pharmacy professionals is an important issue that needs due consideration particularly with respect to confidentiality of patient data, withholding therapeutic interventions and varying cost of drug.

PATIENT ADHERENCE

Patient compliance is the extent to which the patient follows the prescribed medicine regime, while adherence is participation of patients in their care plan resulting in understanding, consent and partnership with the provider. There are different factors which contribute to patients' non-adherence. These factors include:

- Nature of treatment, which in turn depends on: the complexity of the regime (increases with the frequency of administration and number of medicines prescribed) and adverse effects
- Characteristics of the patient, such as: forgetfulness about taking the medication, inability to finish as they feel better, lack of understanding the prescription, fear of dependence, social or physical problems to go to pharmacies, inability to pay prescription charges and inconvenience of taking medicines everyday
- Type of illness, like schizophrenia
- The health care system (long waiting times, uncaring staff, uncomfortable environment, exhausted medicine supply, inaccessibility of health institutions)
- Behavior of prescribers and dispensers: not able to gain confidence from patients, irrational prescribing and dispensing, giving inadequate information on the treatment, poor attitude towards patients, negligence, poor perception to teamwork, absence or ineffective care plan

Patient adherence can be improved by supervising medicine administration; simplifying the therapeutic regime; educating patients on the importance of adhering to the prescribed medication and improving the attitudes of prescribers.

ADVERSE DRUG REACTIONS

Adverse Drug Reactions (ADRs) is a response to a medicine which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological functions. They could be mild (where no intervention is required), moderate (where switching to another medicine is necessary), severe (where an antidote should be employed to alleviate the situation), or lethal. They could also be predictable (extensions of pharmacological effects) or unpredictable (bizarre reactions which are not expected in all patients taking the medicine, such as hypersensitivity and idiosyncratic reactions). ADRs are different from toxic reactions for the latter occur at doses higher than therapeutics. They are also different from side effects as this is a broader concept, i.e., including both beneficial and all unwanted effects which may not necessarily be noxious. The two extreme age groups, i.e., pediatric and geriatric patients, are more susceptible to ADRs due to physiological and pathological factors. Special precaution should be taken for coexisting illnesses, such as kidney and liver diseases, as they could contribute to ADRs. Readers are recommended to refer Ethiopian Guideline for Adverse Drug Events Monitoring (2014).

MONITORING ADRs

Pre-marketing clinical trials cannot be exhaustive as far as detection of all ADRs is concerned due to:

- Recruitment of small populations (often < 2500 patients)
- Low chance of low incidence reactions being picked up before marketing
- Shorter duration of assessment
- Exclusion of patients who may take the medicine post-marketing Only the most common ADRs could be detected during pre-marketing trials. It is therefore, important to devise methods for quickly detecting ADRs. This could be carried out by post- marketing surveillance, i.e., ADR monitoring. All health professionals have the responsibility to report any observed unique adverse reactions from drugs, vaccines or traditional herbal medicine products to Ethiopian Food and Drug Authority (EFDA). (https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=ET).

DRUG/ MEDICINE INTERACTIONS

Drug/medicines interaction is alteration of the response to drugs upon the concurrent administration of other drugs. The interaction includes a reaction between two (or more) drugs or between a drug and a food, drinks, or supplement/herbs. Taking a drug while having certain medical conditions can also cause a drug interaction. Although some medicine interactions could be beneficial, most are harmful.

Hence, it is always important to note the possible medicine interactions prior to concomitant medicine/food or drink administration.

Drug/ Medicine interactions could occur at different levels, including:

- Pharmaceutics, which are physicochemical interactions in an IV infusion or in the same solution;
- Pharmacokinetics, which may take place at the level of absorption, distribution, biotransformation or excretion;
- Pharmacodynamics, which could occur directly at receptor level, or indirectly, where a medicine alters the response to another medicine for example by eliciting opposite physiological effect.

Drug/Medicine interactions could be additive (the effect is simple algebraic sum), synergism (the total effect is more than the algebraic sum), potentiation (the effect of one medicine increases by the presence of another medicine or food), or antagonism (the effect of the agonist is blocked by the antagonist when given together). Medicine interactions are some of the most common causes of adverse reactions. As medicine reactions could also occur between a medicine and food or a medicine and drink. The healthcare provider should always inform patients the type of food or drink which they have to avoid or are recommended to have while taking the medicine.

Medicines should not be added to blood, amino acid solutions or fat emulsions. Some medicines, when added to IV fluids, may be inactivated due to changes in pH, precipitate formation or chemical reactions. For example, benzyl penicillin and ampicillin lose potency after 6-8 hours if added to dextrose solutions, due to the acidity of the solutions. Some medicines, such as diazepam and insulin, bind to plastic containers and tubing. Aminoglycosides are incompatible with penicillin and heparin. Hydrocortisone is incompatible with heparin, tetracycline and chloramphenicol.

PRESCRIBING FOR SPECIAL POPULATIONS

Pharmacotherapy of special groups like pregnant women, children, the elderly and others require consideration of the differences in pharmacokinetics and pharmacodynamics that can significantly affect the safety and efficacy of drugs used in these special populations. Moreover, most randomized controlled clinical trials exclude these groups, which make it difficult for the health professional to make evidence-based decisions regarding appropriate drugs and dosing regimens to use in these patients. Health professionals are recommended to consider the physiological and pathological conditions that affect treatment outcomes in special populations.

PRESCRIBING FOR PREGNANT WOMEN

Pharmacokinetics of a medicine is altered during pregnancy: the rate of absorption decreases, while volume of distribution, metabolism and glomerular filtration rate increase. These phenomena may alter the serum drug level and seen by changes on required response. The embryonic period, where, organogesis takes place, is the most susceptible period to medicine effects. Administration of medicines, except those proved safe, in the first trimester, is therefore not generally recommended. It is advisable not to prescribe any medicine during any stage of pregnancy if possible. This, however, should not preclude the importance of prescribing in life-threatening conditions of the mother. Prior to prescribing any medicine for pregnant women, the benefit risk ratio of prescribing should be considered. Readers are recommended to refer the National Medicines Formulary and Pregnancy Category Guides to select appropriate medicines during pregnancy.

PRESCRIBING FOR BREAST FEEDING WOMEN

Most medicines administered are detectable in breast milk. The concentration, however, is low. If the woman has to take a relatively safe medicine, she should do so optimally 30-60 minutes after breast feeding and 3-4 hours before the next feeding in order to allow time for medicines to be cleared from the blood, and concentration in the breast milk is relatively low. Medicines for which no safety data are available during lactation should be avoided, or breast feeding discontinued while they are administered. Most antibiotics taken by breast feeding mothers can be detected in breast milk. e.g., tetracycline and chloramphenicol. Similarly, isoniazid, sedative hypnotics and opioids enter breast milk sufficient to produce a pharmacologic effect in infants. Antineoplastic medicines are contraindicated in breast feeding.

PRESCRIBING FOR INFANTS/CHILDREN

Physiologic processes that influence medicine kinetics in infants change significantly in the first year of life, especially the first few months, while there is not much difference in the dynamics. All the four processes of pharmacokinetics are, therefore, affect infants/children. Gastric acid secretion begins soon after birth and increases gradually over several hours in full term infants. In premature infants, however, secretion is slower, with the highest concentration occurring on the fourth day. So, medicines, which are partially or totally inactivated by the low pH of gastric content, should not be administered orally. Gastrointestinal enzymes are lower in neonates than in adults. Neonates have less bile acid such that a lipid soluble medicine is absorbed less. Gastric emptying time is prolonged in the first day. Thus, medicines that are absorbed primarily in the stomach may be more fully absorbed. For medicines absorbed in the small intestine, therapeutic effects may be delayed. Peristalsis in neonates is slow. More medicines, therefore, will get absorbed from the small intestine. The volume of distribution is low in children, and medicine metabolizing enzymes are not well developed. The glomerular filtration rate is slower than in adults (30-40%), such that the clearance of medicines is slower in children than in adults. This definitely demands dose adjustment for these age groups.

DOSE ADJUSTMENT IN PEDIATRICS

The most reliable pediatric doses are those given by the manufacturer. If no such information is given, the dose can be calculated using formulae based on age, weight or surface area. Calculations of doses based on age or weight are conservative and tend to underestimate the required dose. Doses based on surface area are more likely to be correct, which makes it the common approach used for dose estimation of cytotoxic chemotherapeutic agents. Pediatric doses can be calculated as follows:

Dose = adult dose*(age in years/(age+12))
Dose calculations based on weight: Dose = adult dose*(weight in kg/70)
Dose calculations based on surface area:

$$\text{Dose} = \frac{[\text{Child surface area}] \times [\text{Adult dose}]}{[\text{Adult body surface area}]}$$

PRESCRIBING FOR ELDERLY PATIENTS

There is no major alteration in medicine absorption in elderly patients. However, conditions associated with age may alter the rate of absorption of some medicines. Such conditions include altered nutritional habits; alteration in gastric emptying (which is often slower); and the concurrent administration of other medicines affecting pH and motility of the gut. Aged people have reduced lean body mass, reduced body water and an increase in fat as a percentage of body mass. There is a decrease in serum albumin, and the ratio of bound to free medicine is significantly changed.

Capacity of liver to metabolize drugs declines with age for some drugs. Phase I reactions carried out by microsomal P450 systems are affected more in elderly patients than phase II reactions. There is a decline with age of the liver's ability to recover from injury. Diseases that affect hepatic function like congestive cardiac failure and nutritional deficiencies are more common in the elderly. Creatinine clearance declines in the elderly leading to marked prolongation of the half-life of medicines excreted by kidney. The increased incidence of active pulmonary disease in the elderly could compromise medicine elimination through exhalation. There is also a change in the sensitivities of receptors to medicines in elderly people. The quality and quantity of life for elderly patients can be improved through the careful use of medicines.

PRESCRIBING IN RENAL FAILURE

Many medicines are excreted through the kidneys and impairment of renal function alters the excretion of these medicines, resulting in renal as well as non-renal toxicity unless doses are adjusted accordingly. There are two principal pathways for medicine excretion by the kidneys; glomerular filtration and tubular excretion. Glomerular filtration plays a major role in the excretion of small, non-protein bound molecules whereas protein bound molecules that are excreted in urine are eliminated by secretion into the proximal tubules.

For dose adjustment in renal failure, it may occasionally be necessary to measure medicine levels and adjust doses accordingly, but generally, doses are adjusted on the basis of the estimated Glomerular Filtration Rate (GFR). Among the various formulae used to estimate the GFR from the serum creatinine, the Cockcroft- Gault (CG) formula is the easiest to use (although not the most accurate) to adjust doses of medications that are eliminated by the kidneys. The GFR in the CG formula is calculated as follows:

$$\text{GFR}= \frac{[140\text{-age}] \times [\text{body weight (kg)}]}{72\text{x } [\text{Serum creatinine in mg/dL}]}$$

The value is multiplied by 0.85 in women to account for smaller muscle mass.

Factors that potentiate renal dysfunction and contribute to the nephrotoxic potential of renally excreted medicines include: i) intravascular volume depletion either due to external losses or fluid sequestration (as in ascites or edema) and ii) concomitant use of 2 or more nephrotoxic agents e.g., Nonsteroidal anti-inflammatory agents, aminoglycosides, radio contrast agents.

To avoid worsening renal dysfunction in the presence of renal impairment:

- Avoid potentially nephrotoxic medicines and use alternative medicines that are excreted through other routes (Medicine formularies and text books tabulate drugs to be avoided or used with caution in patients with renal failure);
- If there are no alternatives, calculate the GFR and adjust the dose on the basis of the estimated GFR (many textbooks, formularies have tables showing dose adjustment on the basis of estimated GFR). Dose adjustment may be accomplished in three different ways:
    i) Decreasing each individual dose and maintaining the same dose frequency;

    ii) Maintaining the same individual dose but administering each dose less frequently; and

    iii) Modifying both individual doses and the frequency of administration, which is a combination method;
- Avoid concomitant use of two or more potentially nephrotoxic agents;
- Ensure that the patient is adequately hydrated;
- If the patient is on dialysis check if the medicine is eliminated by the

specific dialysis modality and consider administering a supplemental dose at the end of the dialysis session;

- Serially monitor kidney function.

PRESCRIBING IN LIVER DISEASE

The liver is a site for the metabolism and elimination of many medicines but it is only with severe liver disease that changes in medicine metabolism occur. Unfortunately, routine determination of liver enzymes and other tests of liver function cannot predict the extent to which the metabolism of a certain medicine may be impaired in an individual patient.

In general terms medicine prescription should be kept to a minimum in all patients with severe liver disease as it may alter the response to medicines in several ways. Major problems occur in patients with advanced liver disease who have ascites, jaundice or hepatic encephalopathy:

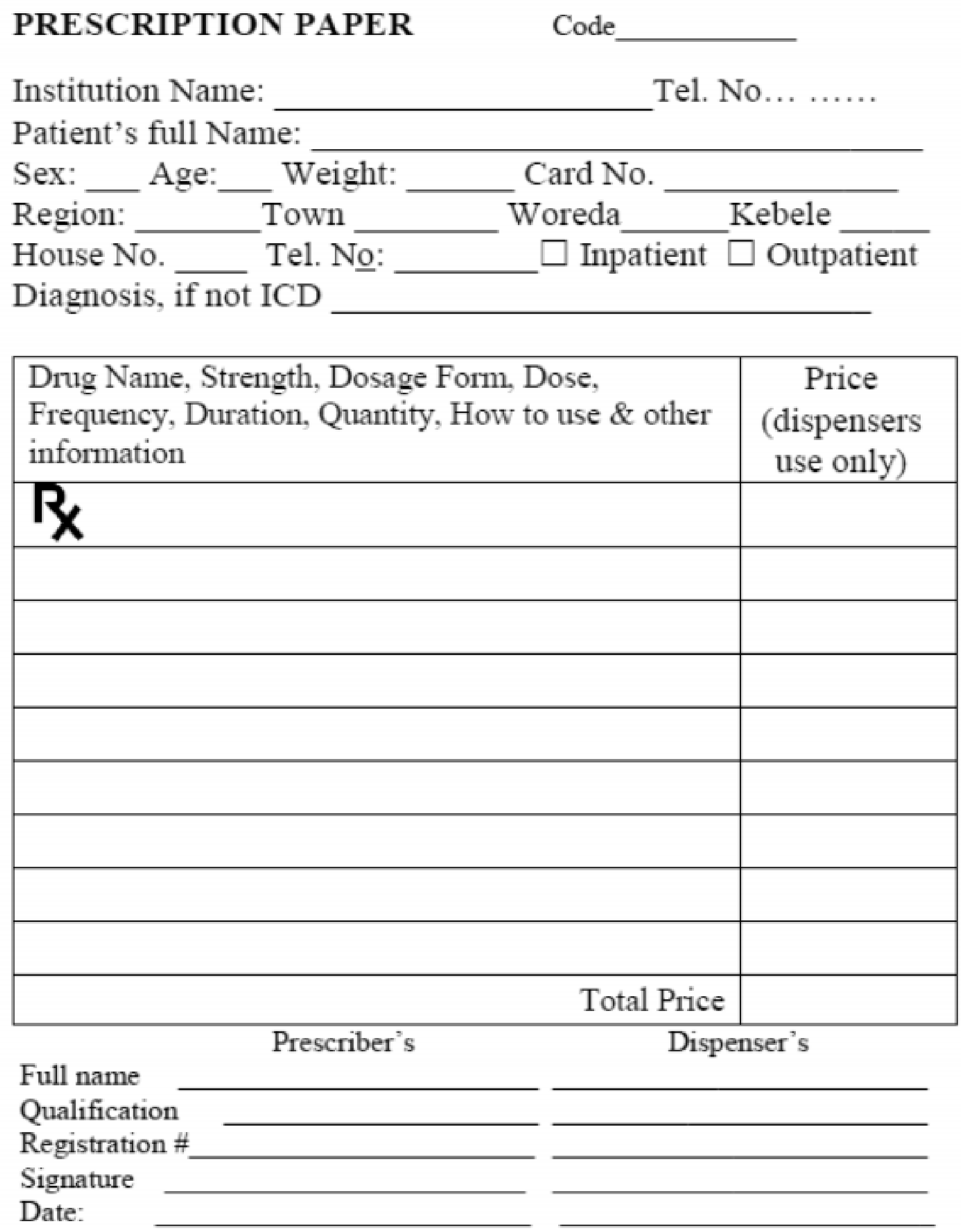
- The hypoproteinemia in patients with severe liver disease is associated with reduced protein binding and increased toxicity when highly protein bound medicines are used.
- One must exercise caution in the use of some medicines like sedatives, opioids and diuretics which may precipitate hepatic encephalopathy in patients with advanced liver disease.

It is always advisable to consult tables in standard textbooks or medicine formularies before prescribing medicines for patients with severe liver disease.

NARCOTIC AND PSYCHOTROPIC DRUGS: CONTROLLED SUBSTANCES

Prescribing a medicine that is liable to abuse requires special attention and may be subject to specific legal requirements. Authorized health workers must use these medicines responsibly. The strength, directions and quantity of the controlled substance to be dispensed should be stated clearly. Required details must be filled in the special prescription form carefully to avoid alteration and abuse. Readers are recommended to refer the National List of Psychotropic Substances and Narcotic drugs (2017) that contain the list of psychotropic substance and narcotic drugs under national control to assist health professional in promoting rational drug use of psychotropic substance and narcotic drugs.

Annex: Standard prescription form



PRESCRIPTION PAPER Code____________

Institution Name: _________________________Tel. No… ……
Patient's full Name: ____
Sex: ___ Age:___ Weight: _______ Card No. _______________
Region: ________Town _________ Woreda_______Kebele _____
House No. _____ Tel. No: _________☐ Inpatient ☐ Outpatient
Diagnosis, if not ICD ___________________________________

Drug Name, Strength, Dosage Form, Dose, Frequency, Duration, Quantity, How to use & other information	Price (dispensers use only)
℞	
Total Price	

	Prescriber's	Dispenser's
Full name	________________________	________________________
Qualification	________________________	________________________
Registration #	________________________	________________________
Signature	________________________	________________________
Date:	________________________	________________________

CHAPTER 2:

ANTIMICROBIAL RESISTANCE AND ITS CONTAINMENT

OVERVIEW OF ANTIMICROBIAL RESISTANCE (AMR)

Infectious diseases are those which are caused by microorganisms like bacteria, protozoa, viruses and fungi. These diseases are threats to all societies irrespective of age, gender, ethnicity, education and socioeconomic status. Unexpected outbreaks of infectious disease can occur at any time and at any place resulting in high morbidity and mortality. Their treatment imposes a huge financial burden to societies, especially developing ones. On top of these problems, antimicrobial resistance (AMR) can easily emerge through microorganisms in medicines used for the treatment of infectious diseases, known as antimicrobials. AMR is the ability of microorganisms to survive and/or multiply in the presence of tolerable doses of antimicrobial medicines. AMR may be natural when it occurs spontaneously as a result of gene mutation, or may be acquired due to inappropriate exposure to antimicrobials.

There are different definitions used to describe various forms of AMR. These include:

- Multidrug resistant (MDR) was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories,
- Extensively drug resistant (XDR) was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two categories)
- Pan-drug resistant (PDR) was defined as non-susceptibility to all agents in all antimicrobial categories,
- Cross-resistance refers occurs of resistance among other (different) antimicrobials as a result of exposure to a similarly acting antimicrobial
- Co-resistance refers to resistance to more than one class of antibiotics in the same bacterial strain as might occur on a plasmid.

FACTORS WHICH CONTRIBUTE TO ANTIMICROBIAL RESISTANCE

Antimicrobials are the most misused medicines in many developing countries like Ethiopia. They are available not only over the counter (OTC) in pharmacies but also in open markets. Studies indicate the most common medicines used for self-medication are antibacterials. There are a number of factors responsible for resistance to emergence. Some of them include:

- Poor infection prevention and control; poor waste management (environment contamination with antimicrobials)
- Irrational prescribing, Irrational dispensing and irrational use (non-compliance, self-medication, sharing)
- Irrational use of antimicrobials in agriculture (animal feeds, crop production). Currently, antimicrobials are irrationally used for the treatment of zoonosis, prophylaxis and growth promotion of food for animals.

MECHANISMS FOR ANTIMICROBIAL RESISTANCE

There are several mechanisms by which microorganisms develop AMR. These include:

A. Inability of antimicrobials to concentrate on their targets by:
    a) Denying access to their sites of action, e.g., Resistance to cephalosporins;
    b) Increasing their efflux e.g., Resistance to tetracycline.

A. Inactivation of antimicrobials through;
    a) Production of degrading enzymes like β lactamases which hydrolyze β lactams, e.g., resistance to penicillin; and medicine bio transforming enzymes, e.g., resistance to chloramphenicol;
    b) Inducing bacterial failure to convert a pro-medicine to active metabolites, e.g., resistance to INH.

A. Alteration of targets, due to:
    c) Target modification, e.g., macrolide resistance;

d) Substitution with a resistant target to the native agent e.g., methicillin resistance;

e) Use of alternate metabolic pathways, e.g., sulfonamides resistance;

f) Mutation of the natural target, e.g., fluoroquinolone resistance.

THREATS OF ANTIMICROBIAL RESISTANCE (AMR)

Many important medicine options for the treatment of common infectious diseases are becoming limited, expensive or cease to exist. Today, nearly all Staphylococcus aureus strains are resistant to penicillin. Resistance to methicillin and also vancomycin is also increasingly observed. If it is not possible to limit emergence and/or spread of AMR, infections may become untreatable.

AMR has several economic and health impacts. They cause prolonged illness, absence from work and reduced productivity. AMR can also contribute towards longer hospital stay which increases cost. AMR prolongs the period of infectiousness resulting in spread of infection, ultimately impacting mortality rates.

ANTIMICROBIAL RESISTANCE (AMR) IN ETHIOPIA

Ethiopia published the first AMR baseline surveillance in 2009 (http://www.fmhaca.gov.et/wp-content/uploads/2019/03/AMR_Baseline_Survey.pdf). The data was generated form routine surveillance of public hospitals carried from 1996 to 2000.A total of 52, 682 culture records were retrospectively reviewed, of which 18, 466 have growth and sensitivity tests done and were included in the analysis. Although, the collected data suffer from a small number of isolates in majority of case, considerable degree of resistance to commonly used first line antibacterial over the five-year period was observed as shown below.

Pathogen	Increase in resistance from 1996 to 200	Resistance data from systematic reviews discussed below
Coagulase negative staphylococcus	Erythromycin resistance 21.6% in 1996 to 51.9% in 2000	Erythromycin: 37% (95% CI: 21, 55%)
Streptococcus pneumonia	Erythromycin resistance from 0% in 1996 to 18.2% in 2000	
	chloramphenicol resistance 0% in 1996 to 17.4 % in 2000	
Salmonella species	Cotrimoxazole resistance 33.3% in 1997 to 62.5% in 2000	Cotrimoxazole: 68.01%
Staphylococcus aureus	methicillin resistance 87.5% in 1996 to 100% in 2000	

COAGULASE NEGATIVE STAPHYLOCOCCUS (CONS)

Based on 2018 systematic review, Coagulase negative staphylococcus (CoNS) resistance to vancomycin (9.11%[95% CI: 0, 35%]), clindamycin (11% [95% CI: 2, 27%]) and ciprofloxacin (14%[95% CI: 6, 22%]) relatively lower than all other agents like penicillin's (including amino and anti-staphylococcus penicillin's), cephalosporin's, tetracycline's, macrolides, chloramphenicol, and cotrimoxazole (https://pubmed.ncbi.nlm.nih.gov/29801462/).

SALMONELLA SPECIES

The 2014 Salmonella systematic review reported a progressive increase in the odds of multi-drug resistant isolates in the early 2000s as compared to the late 1990s (OR =18.86, 95% CI = 13.08, 27.19). Among the tested drugs, resistance was low for ciprofloxacin (3.61%). The pooled proportions of ampicillin, co-trimoxazole, chloramphenicol, and multi-drug resistant isolates in the 2000s were 86.01%, 68.01%, 62.08%, and 79.56% respectively. (https://pubmed.ncbi.nlm.nih.gov/25213011/).

SHIGELLA SPECIES

A systematic review and meta-analysis of 25 studies (published from 1999 to 2018) that assessed stool samples of 8521 patients (including community cases) was published in 2019. The pooled prevalence of Shigella species was 6.6% (95% CI 4.7-8.8) (https://pubmed.ncbi.nlm.nih.gov/31288806/), i.e 8.5%, 95% CI (6.2-11.5) among patients in Health facility and 1.6%, (95% CI 0.8-3.4) in Community based studies. Shigella species were highly resistant (>80% for each) for Tetracycline, ampicillin, amoxicillin and erythromycin (see some of the figures in the right column of above table). The MDR rate is 83.2% (95% CI 77.1-87.9). On the other hand, <10% resistance was reported for each ciprofloxacin, ceftriaxone, and norfloxacin. Resistance to aminoglycosides is between 10 to 20%. Subgroup analyses indicated that study years were associated with a decreasing Shigella prevalence over time (p = 0.002).

ESCHERICHIA COLI

Based on 2018 systematic review of 35 studies (most of the studies utilized specimens for screening particularly with multisite swabbing), *E. coli* antibacterial resistance was 45.38% (95% CI: 33.50 to 57.27). Greater than 50% resistance was noted for aminopenicillins (>80% R), cotrimoxazole, tetracycline, Erythromycin and cephalexin. Resistance to fluoroquinolones, third generation cephalosporin's and aminoglycosides was less than 50% (but >20%). The only agent showed < 20% was nitrofurantoin (https://pubmed.ncbi.nlm.nih.gov/29854757/). Similarly, 24.3% fluoroquinolone resistance was observed for *E. coli* in a review published in 2018 (https://pubmed.ncbi.nlm.nih.gov/30541613/). This study also reported high fluoroquinolone resistance for Neisseria gonorrhea (48.1%) and Klebsiella pneumonia (23.2%). All these are an alarmingly report that loom out the traditional empiric decision. Hence, infection prevention measures will be crucial (see additional details about ESBL-producing grave pathogens like *E. coli* below).

MAGNITUDE OF MULTIDRUG RESISTANT INFECTIONS IN ETHIOPIA

Recent systematic review and meta-analysis were conducted for different grave infections like Extended-spectrum beta-lactamase (ESBL)-producing gram negative bacteria, Vancomycin resistance enterococci (VRE), Methicillin resistant Staphylococcus aureus (MRSA) and multidrug resistant tuberculosis

(MDR TB). All the pooled estimates were based on highly heterogeneous data. The data of the majority of these reviews were generated form in-patients and high level hospitals and research laboratories (See table below) and need to be interpreted cautiously for the settings where this guideline is intended to be used. In addition, data from emerging regions were largely missed. Hospital with microbiology laboratories should better relay on their setting specific surveillance data. Future national or regional (especially community based is lacking) surveillance should be carried for a better decision.

EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING GRAMNEGATIVE ORGANISMS

A 2020 systematic review and meta-analysis of 14 studies assessed 1649 Gram-negative bacteria isolated from 5191 clinical samples for ESBL-producing pathogens (https://aricjournal.biomedcentral.com/articles/10.1186/s13756-020-00782-x). Despite high level of data heterogeneity ($I^2 = 95\%$, $P < 0.01$), the pooled proportion of ESBL-producing Gram-negative bacteria was **50%** (95% CI: 47.7–52.5%. Specifically, 65.7% (n = 263) for Klebsiella spp., 62.2% (n = 33) for Enterobacter spp., 48.4% (n = 90) for Salmonella spp., 47.0% (n = 383) for E. coli, 46.8% (n = 22) for Citrobacter spp., 43.8% (n = 7) for Providencia spp., 28.3% (n = 15) for Proteus spp., 17.4% (n = 4) for Pseudomonas aeruginosa, 9.4% (n = 3) for Acinetobacter spp., and 20.8% (n = 5) for other Gram-negative bacteria, respectively. ESBL-encoding genes were found in 81 isolates: 67 isolates harbored the CTX-M-1 group and 14 isolates TEM. The mortality associated with infections by bacteria resistant to third generation cephalosporins has reported only in two included studies, reaching 33.3% (1/3) and 100% (11/11). (See table below)

VANCOMYCIN RESISTANCE ENTEROCOCCI (VRE)

A recent systematic review and meta-analysis included 20 studies. In this study among 831 *enterococci,* 71 VRE isolates were identified. The pooled VRE estimate accounts 14.8% (95% CI; 8.7–24.3; I2 = 74.05%; P < 0.001) (https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-4833-2).(see table below)

METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

MRSA accounts 32.5% (95% CI, 24.1 to 40.9%; I2 = 96%, P < 0.001). MRSA strains were >97% resistant to penicillin, ampicillin, erythromycin, and amoxicillin. On the other hand, have low resistance (5.3%) to vancomycin (https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-016-2014-0). (see table below)

MDR TB IN ETHIOPIA

The prevalence of MDR TB among newly diagnosed patients was 2.7% as per the first national prevalence survey of Ethiopia (https://pubmed.ncbi.nlm.nih.gov/24903931/). Recent meta-analysis in 2017 and 2018 reported 2% (95% CI 1% - 2%) (https://pubmed.ncbi.nlm.nih.gov/28320336/) and 2.18% (95% CI 1.44–2.92%) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6000958/), respectively. This same meta-analysis reported a prevalence of 15% (95% CI 12% - 17%) and 21.07% (95% CI 11.47–30.67%) among previously treated patients. MDR-TB is mainly associated with history of previous treatment and to a lesser extent with contact history. As per the 2018 systematic review MDR TB accounted for the pooled death computed among 5 articles showed that 12.25% (95% CI 9.39–15.11%) death. Complication, drug side effects and HIV infection were the main determinants for the death. (See the table below)

Resistant Pathogens	Prevalence of resistance	Settings and period	Methods	Specimen
ESBL-RE	50% (95% CI: 0.48–0.52, I^2 = 95%, $p < 0.01$);	In-patient and/or outpatient departments of tertiary hospitals; 2003 to 2017.	Double Disk Synergy Test & both DDST and PCR	urine & multisite (stool, swabs, sputum, blood & fluids)
Enterococcus (VRE)	14.8% (95% CI; 8.7–24.3; I^2 = 74.05%; $P < 0.001$), High in AA and Amhara	Hospital patients, except one; Amhara, Oromia, AA and SNNP; 2013 to 2018	Disc diffusion or Dilution/ MIC	Stool and multisite (stool urine, blood & swab)

Staphylococcus (MRSA)	32.5% (95% CI, 24.1 to 40.9%; I2 = 96%, P < 0.001); Vanco resistance = 5.3% (0–10.6)	Mixed (in- and outpatients) studies, except 13.8% for school children, 2004 to 2014	Not Available	Multisite swab
MDR-TB	7.24% (95% CI 6.11-8.37); I2=98.4%, p=0.000; 2.18% (95% CI 1.44–2.92%) of newly diagnosed and 21.07% (95% CI 11.47–30.67%) of previously treated	Except one, all are institution-based studies; 1997 and 2017	--	--

NATIONAL RESPONSE TO ANTIMICROBIAL RESISTANCE

In response to the alarming rise in AMR, Ethiopia under took the following progressive and key steps to combat AMR:

- Synthesized the first AMR surveillance data in 2009. http://www.fmhaca.gov.et/wp-content/uploads/2019/03/AMR_Baseline_Survey.pdf
- Developed the national strategy for prevention and containment of AMR. http://www.fmhaca.gov.et/wp-content/uploads/2019/03/Strategy-for-the-Prevention-and-Containment-of-AMR-in-Ethiopia-Oct-2015.pdf.
- Developed a Practical Guide to Antimicrobial Stewardship implementation in Ethiopian Hospitals, MOH, 2018. https://www.ghsupplychain.org/practical-guide-antimicrobial-stewardship-ethiopian-hospitals
- Ethiopian public health institute (EPHI) started to coordinate, perform and report an annual AMR surveillance across the country, since 2017 (16 sentinel sites). This surveillance so far produced two reports.

CONTAINMENT STRATEGIES OF AMR

Key strategies for antimicrobial containment include:

- Optimizing prescribing, dispensing and use of antimicrobials through stewardship (All healthcare settings in Ethiopia should have customized stewardship interventions in place)
- Strong infection prevention and control strategies and practices (All healthcare settings in Ethiopia must have national IPC polices in practice)
- Surveillance: Keeping track of a resistance profile (antibiogram data) in the healthcare institution to help identify the most prevalent pathogens, status of resistance, and appropriate choices of treatment (All healthcare settings in Ethiopia where microbiologic laboratories are available should have a regularly updated antibiogram data)
- Research: conducting and reporting antimicrobial consumption pattern (proper prescribing, dispensing and utilization practices) of the healthcare setting or ward (All healthcare settings in Ethiopia should encourage their staffs and students to carry antimicrobial utilization studies in their healthcare context for an appropriate action).
- Raising awareness (All healthcare settings in Ethiopia should prepare AMR and containment awareness operations to the management, clinicians, students, patients and the larger public)
- Through collaborative/multidisciplinary engagement (physicians, nurses, pharmacists, microbiologists, infection prevention and control team, healthcare management, bureau and ministry)

ANTIMICROBIAL STEWARDSHIP PROGRAM (ASP)

- Antimicrobial stewardship (AMS) is defined as an organizational or healthcare system-wide approach for promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness. ASP is recognized globally as a key strategy to manage inappropriate use of antibiotics.

PROSPECTIVE AUDIT AND FEEDBACK

- A prospective audit and feedback system involves a multidisciplinary team who regularly reviews patients.

FORMULARY RESTRICTION AND PRE-AUTHORIZATION

- Preauthorization is a strategy to improve antibiotic use by requiring clinicians to get approval for certain antibiotics before they are prescribed. A list of restricted antimicrobials (Watch and Reserve) would need to be included in the hospital antimicrobial policy which will be reviewed on regular basis.

ACCESS, WATCH AND RESERVE (AWARE) CLASSIFICATION OF ANTIBIOTICS

AWaRe stands for **ACCESS, WATCH** and **RESERVE**. It is an antibiotic classification system introduced in 2017 by The World health Organization (WHO) Essential medicine list (EML). It was first introduced in 2020 in the Ethiopian Essential Medicine List (EEML-2020). The classification is aimed to promote rational antibiotic use and provide a tool for antimicrobial stewardship (AMS) activities and monitoring of antimicrobial consumption. The AWaRe classification implementation aims to enhance the health facility's ability to contribute to the national antibiotic consumption and to reduce use of the antibiotics most at risk of resistance from the Watch and Reserve groups. Hence this will help to contain antimicrobial resistant by:

- Strengthening the capacity of the health-care facility's ASP to implement AMS
- Aligning empirical antibiotic treatment with ACCESS antibiotics;
- Targeting WATCH and RESERVE groups for AMS;
- Reviewing antimicrobial consumption and use surveillance data with AWaRe approach;

ACCESS GROUP ANTIBIOTICS

- Have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistance potential than antibiotics in Watch and Reserve groups.
- Widely used as first- or second -choice empiric treatment options for specified infectious syndromes.
- Should be widely available, affordable and quality-assured to improve access and promote appropriate use.

WATCH GROUP ANTIBIOTICS

- Have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials (CIA) for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance.
- Widely used as first- or second -choice empiric treatment options for specified infectious syndromes.
- Should be prioritized as key targets of hospital stewardship programmes and monitoring.
- Use in animal health and food production must be highly regulated

RESERVE GROUP ANTIBIOTICS

- Should be reserved for treatment of confirmed or suspected infections due to multi drug-resistant organisms, and treated as "last-resort" options.
- They should be accessible, but their use should be tailored to highly specific patients and settings, when all alternatives have failed or are not suitable.
- They must be protected and prioritized as key targets of hospital stewardship programmes, involving monitoring and utilization reporting, to preserve their effectiveness.
- Used when they have a favorable risk-benefit profile and proven activity against "Critical Priority" or "High Priority" pathogens identified

by the WHO Priority Pathogens List, notably carbapenem resistant Enterobacteriaceae.

Table 2.1: AWaRe classification of antibiotics in the EEML-2020

Group		
Access	Watch	Reserve
1. Amoxicillin 2. Amoxicillin + Clavulanic Acid 3. Ampicillin 4. Penicillin G, Benzanthin 5. Penicillin G, Sodium Crystalline 6. Cloxacillin 7. Cephalexin 8. Cefazolin 9. Azithromycin 10. Clarithromycin 11. Sulphamethoxazole + Trimethoprim 12. Nitrofurantoin 13. Norfloxacin 14. Gentamicin 15. Metronidazole 16. Doxycycline	1. Ampicillin + Sulbactam 2. Cefuroxime 3. Cefixime 4. Cefpodoxime Cefotaxime Sodium 5. Ceftriaxone 6. Ceftazidime 7. Cefepime 8. Ceftriaxone + sulbactam 9. Ciprofloxacin 10. Clindamycin	1. Piperacillin + tazobactam 2. Meropenem 3. Meropenem + Vaborbactam 4. Ceftazidime + Avibactam 5. Colistin 6. Polymyxin B Vancomycin

FURTHER READING

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2. Global antimicrobial resistance surveillance system (GLASS) report: early implementation 2020. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO (https://apps.who.int/iris/bitstream/handle/10665/332081/9789240005587-eng.pdf?ua=1)
3. The selection and use of essential medicines: World Health Organization technical report series. Geneva: World Health Organization; 2017. (https://www.who.int/medicines/publications/essentialmedicines/EML_2017_EC21_Unedited_Full_Report.pdf)

4. Executive summary: the selection and use of essential medicines 2019. Geneva: World Health Organization; 2019.

5. https://adoptaware.org/

HOSPITAL ACQUIRED INFECTION (HAI) PREVENTION MEASURES

The goal of infection control is to prevent and reduce rates of resistant hospital acquired (nosocomial) infections. Please visit Ethiopian infection prevention guideline for healthcare facilities: https://agris.fao.org/agris-search/search.do?recordID=US2012413697. The CDC also has infection prevention toolkits that can be adapted to our settings (https://www.cdc.gov/hai/prevent/prevention_tools.html)

MEASURES AT EACH HEALTHCARE LEVEL

Every health setting should have 1) infection prevention and control team. 2) Provide ongoing training and retraining of staff with responsibility for cleaning and disinfection, 3) standardized cleaning process/IPC protocol, monitoring and feedback strategies to decrease the risk of infection. It would be good if the protocol is based on the surveillance of the health settings infection volume or potential. As well, Health Care Waste Management (including pharmaceutical waste management) should be one core quality indicator for IPC (http://www.fmhaca.gov.et/wp-content/uploads/2019/03/Healtcare-Waste-management.pdf).

CORE INFECTION CONTROL MEASURES IN HEALTH CARE SETTINGS

- Early recognition and reporting
- Infection control precautions (Standard precautions, Transmission-based precautions)
- Cleaning, disinfection and sterilization of medical equipment-according to equipment type.
- Hand hygiene: alcohol-based hand rub, hand washing with soap and water

- Personal Protecting Equipment (PPE): gloves, gowns, masks/respirators, eye protection
- Patient accommodations and care (bed spacing)
- Environmental cleaning, disinfection and waste disposal: removal of organic material on soiled surfaces followed by disinfection, which eliminates microorganisms and proper disposal. Better performed by public health or environmental science professionals
- Occupational health management

PRECAUTIONS TO INFECTION PREVENTION

Precautions for preventing transmission of infection include standard precautions and additional precautions which include isolation (contact, airborn) precautions. **Standard Precautions** are guidelines designed to create a physical, mechanical, or chemical barrier between microorganisms and a person (patients and health care workers) to prevent the spread (break the chain) of infection and reduce the risk of pathogen transmission in hospitals.

Examples of Barriers:

- **Physical**: PPE (gloves, face masks, goggles, gowns, plastic or rubber aprons, and drapes)
- **Mechanical**: HLD by boiling or steaming and sterilization by autoclaving or dry heat ovens
- **Chemical**: Antiseptics (alcohol-based antiseptic agents) and high-level disinfectants (chlorine and glutaraldehydes)

STANDARD PRECAUTIONS

The following standard precautions should be performed for the care of all patients:

- Hand hygiene before and after every patient contact with soap and water (preferred for norovirus and C. difficile infection over ABHR) or alcohol-based hand rub (ABHR)… single most important measure to reduce transmission.

- Use of gloves, gowns, and eye protection (for situations in which exposure to body fluids is possible); glove use should never be a replacement for hand washing.
- Use of respiratory hygiene/cough etiquette: Patients and caretakers should cover their nose or mouth when coughing, dispose used tissues immediately, and exercise hand hygiene after contact with respiratory secretions.
- Safe disposal of sharp instruments in impermeable containers.
- Safe disposal or cleaning of instruments and linen.
- Routinely cleaning and disinfecting equipment and furniture in patient care areas
- Using safe work practices

Isolation precautions: Must be practiced in addition to the standard precautions above.

Carried based on main modes of microorganism transmission in healthcare settings: contact, droplet, and airborne spread

CONTACT PRECAUTION

- Contact precautions are recommended for Colonization of any bodily site with multidrug-resistant bacteria (MRSA, VRE, ESBL producing), Enteric infections (Norovirus, Clostridioides difficile, Escherichia coli), Viral infections (HSV, VZV, RSV, parainfluenza, rhinovirus, enterovirus, certain coronaviruses [e.g., COVID-19, MERS-CoV]), Scabies, Impetigo, Non-contained abscesses or decubitus ulcers (especially for Staphylococcus aureus and group A Streptococcus).

DROPLET PRECAUTIONS

- Droplet precautions are suggested for known or suspected bacterial infections (Neisseria meningitides, Haemophiles influenzae type B, Mycoplasma pneumonia, Bordetella pertussis, Group A Streptococcus, Diphtheria, Pneumonic plague), viruses (Influenza, Rubella, Mumps, Adenovirus, Parvovirus B19, Rhinovirus, Certain coronaviruses).

AIRBORNE PRECAUTIONS

- Airborne precaution is recommended for known or suspected Tuberculosis, Varicella, Measles, Smallpox, Certain coronaviruses and Ebola.

PREVENTION OF SURGICAL SITE INFECTION (SSI)

- ○ Appropriate administration of effective preoperative antibiotics – most important (see 'Antimicrobial prophylaxis in surgery' section)
- ○ Other perioperative control measures. Use alcohol-containing (with chlorhexidine gluconate or an iodophor) preoperative skin preparatory agents if no contraindication exists. Avoid alcohol in areas that pool or not dry (e.g., involving hair) due to fire risk, procedures involving mucosa, cornea, or ear. In absence of alcohol, chlorhexidine gluconate has advantages over povidone-iodine, for longer residual activity and activity in the presence of blood or serum
- ○ Careful infection control is essential; hand hygiene and use of gloves and other barrier devices (masks, caps, gowns, drapes, and shoe covers) by all operating room personnel. Antiseptics to the skin to reduce burden of skin flora.
- ○ Patients with evidence of active infection prior to elective surgical procedures should complete treatment for the infection prior to surgery, particularly in circumstances when placement of prosthetic material is anticipated. For circumstances in which urgent surgery is required, the Weight risk of infection with the timing of surgical intervention on an individual basis.
- ○ *Staphylococcus aureus* screening and decolonization may be reasonable for surgical patients known to be nasal carriers of *S. aureus* with a high risk of undesirable outcomes if *S. aureus* SSI develop (e.g., cardiothoracic surgery, orthopedic procedures with hardware implantation, immunocompromised patients).
- ○ Wound protectors (impervious plastic sheath) are required for clean-contaminated, contaminated, and dirty abdominal procedures (GI and biliary tract surgeries).

- If hair removal is essential, remove it outside the operating room using clippers or a depilatory agent. Do not use razors as possible.
- Controlling blood glucose (180mg/dL or lower) during immediate postoperative period for cardiac surgery patients is critical. Non-cardiac surgery patients may also benefit.
- Maintaining **peri-operative** normothermia (temperature of 35.5°C or more) decreases SSI.
- Perioperative high-inspired (supplemental) oxygen during and immediately following surgical procedures reduces the risk of SSI. Supplemental oxygen is recognized in patients undergoing surgery with general anesthesia using mechanical ventilation. It is most effective if combined with additional schemes to improve oxygenation, like normothermia and appropriate volume replacement.

PREVENTION OF INFECTION IN THE INTENSIVE CARE UNITS (ICUs)

In ICU, Comorbid conditions, long hospital courses, frequent contact with health care personnel, indwelling catheterization, and receipt of antimicrobial therapy all increase the risk of colonization and infection with multidrug-resistant pathogens (e.g., MRSA, VRE). Infections with such organisms are associated with increased mortality, length of stay, and hospital costs.

Measures to prevent spread of resistant organisms in the ICU include:

- Infection control measures such as good hand hygiene compliance,
- contact precautions for patients for drug-resistant organisms, and
- Minimizing unnecessary hospitalization and interventions.
- Adequate and standardized environmental cleaning and disinfection.
- Antimicrobial stewardship program can decrease selective pressure that promotes emergence of resistant bacterial strains
- More intensive infection control interventions to reduce colonization pressure include:

PREVENTION OF CATHETER-ASSOCIATED URINARY TRACT INFECTIONS (UTI)

- Avoid unnecessary urinary catheterization. Limiting use to appropriate indications is important in minimizing catheter-related complications like infection. Catheters are not indicated for determining the residual volume of urine, or in the management of most patients with urinary incontinence. Urinary catheters are used selectively for operative patients based upon the nature (i.e., pelvic surgery) and duration of the procedure, or need for perioperative fluid monitoring.
- Use sterile technique (e.g., avoid touching the tip) when placing the catheter,
- Remove catheters as soon as possible (preferably in the recovery area or when no longer indicated). However, catheters inserted for surgery on the urinary tract need approval of the surgeon (urologist) to remove.
- Considering alternatives to indwelling urethral catheters. For bladder emptying dysfunction, intermittent catheterization can be used over chronic indwelling catheters. External catheters are preferred over urethral catheters whenever possible for male patients with no evidence of urinary retention or bladder outlet obstruction.
- Not routinely replace urethral catheters: Indwelling urethral catheters and drainage systems are changed only for a specific clinical indication such as infection, obstruction, or compromise of closed system integrity.
- Adequate training of healthcare staff, patients, and caregivers on catheter placement and management is important.
- No clear benefit of using antibiotic-coated urinary catheters or prophylactic antibiotics to reduce the risk of catheter associated urinary tract infection. So not recommended.

PREVENTING VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

Practices that are recommended for preventing VAP include (i.e., decreases average duration of mechanical ventilation, length of stay, mortality, and/or costs; benefits likely outweigh risks):

- Use noninvasive positive pressure ventilation in selected populations

- Manage patients without sedation whenever possible
- Interrupt sedation daily
- Assess readiness to extubate daily
- Perform spontaneous breathing trials with sedatives turned off
- Facilitate early mobility
- Utilize endotracheal tubes with subglottic secretion drainage ports for expected greater than 48 or 72 hours of mechanical ventilation
- minimizing pooling of secretions above the endotracheal tube cuff,
- Change the ventilator circuit only if visibly soiled or malfunctioning
- Elevate the head of the bed to 30 to 45°

PREVENTION OF INTRAVASCULAR CATHETERS ASSOCIATED INFECTION

All types of intravascular catheters are associated with a risk of both local infection and catheter-related bloodstream infection (CRBSI). General measures for prevention of infections associated with any intravascular catheter include:

THE SITE CHOSEN FOR CATHETER PLACEMENT CAN INFLUENCE THE INFECTION RISK.

- Placing peripheral intravenous catheter in the upper extremity rather than the lower extremity is strongly preferred.
- Avoid femoral site for insertion of central venous or pulmonary artery catheters in adults, if possible due to high risk of infection. Internal jugular vein or subclavian veins are preferred.

REPLACEMENT OF INTRAVASCULAR CATHETERS

- Remove any intravascular catheter that is no longer essential. The risk of infection increases with the duration, increasing after more than three to six days at all catheter sites.

- Peripheral intravenous catheters be removed or replaced as clinically indicated, rather than routine removal or replacement after a designated time period.
- Always ensure aseptic technique. If adherence to aseptic technique cannot be assured (such as in emergent catheter placement requirement), replace catheter as soon as possible (and no longer than 48 hours after insertion).
- Central venous catheters, pulmonary artery catheters, and peripheral arterial catheters should be removed as soon as clinically feasible. Routine replacement of these catheters is not praised.
- When central venous catheters are replaced, use of guidewire exchange techniques is not recommended as the approach increases the risk of bloodstream infection.
- Use of antimicrobial-impregnated catheters is good, especially useful in ICUs with high bloodstream infection rates than other comparable units.

REPLACEMENT OF ADMINISTRATION SETS

- Replace administration sets, including secondary sets and add-on devices, no more frequently than at 72-hour intervals, unless clinically indicated.
    - Replace tubing used to administer blood, blood products, or lipid emulsions within 24 hours of initiating the infusion.
    - Replace tubing used to administer propofol infusions every 6 to 12 hours, depending on its use, per the manufacturer's direction.

CATHETER SITE CARE

- Disinfect clean skin with an appropriate antiseptic before catheter insertion and at the time of dressing changes. The antiseptic should air dry before catheter insertion. A 2% chlorhexidine-based preparation is preferred, but there is no recommendation for its use in infants less than two months of age.
- Use sterile gauze or sterile transparent semipermeable dressing to cover the catheter site.
- Do not use topical antibiotic ointment or creams on insertion sites

(except for dialysis catheters).

- ○ Avoid femoral insertion site.
- ○ Prompt removal of catheters when no longer indicated.
- ○ Complications must be watched by examine the catheter site at least once each day. Check every 8-12 hours for phlebitis or evidence of infection.

INTRAVENOUS INJECTION PORTS

- ○ Clean injection ports with 70% alcohol or an iodophor before accessing the system.

PARENTERAL FLUIDS

- ○ Complete the infusion of lipid-containing solutions within 24 hours of hanging the solution.
- ○ Complete the infusion of lipid emulsions alone within 12 hours of hanging the solution.
- ○ Complete infusions of blood or other blood products within 4 hours of hanging the blood.

HEALTH CARE WORKER EDUCATION AND TRAINING

- ○ Educate regarding indication for intravascular catheter use, proper procedures for insertion and maintenance, and infection control measures to prevent intravascular catheter-associated infections.
- ○ Antibiotic lock therapy may be applied for patients with long-term catheters and a history of recurrent CRBSI despite adherence to other routine infection prevention measures.

PREVENTING MATERNAL AND NEWBORN INFECTIONS

The following prevention efforts are being recommended to successfully reduce the risk of fetal and newborn infections:

- Maternal immunization (Tetanus Toxoid)

- Antenatal treatment of maternal syphilis, gonorrhea and Chlamydia infections.
- Prophylactic use of postnatal eye drops to prevent chlamydia, gonorrhea and candida eye infections
- Prophylactic treatment of pregnant women at risk of group B streptococcal disease and
- Maternal and newborn treatment with antiretroviral to prevent mother-to-child transmission of HIV.

FURTHER READING

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CHAPTER 3:

CARE OF PATIENTS IN AMBULATORY AND HOSPITALIZED SETTING

1.1. Clinical evaluation and communication in the outpatient setting

- The overall goal of clinical care is to reach to accurate diagnosis, cure or improve the condition, address the concerns of the clients (patients and families), improve the functional status and sense of wellbeing of the patient.
- Clinicians envisage seeing a satisfied patient and family, improved or cured patient, and trustful continued relationships.
- Accomplishing the above goal requires a strong patient-clinician partnership. The key element for establishing this relationship is good communication.
- The practice of medicine is much more than ordering a set of tests, reaching to a diagnosis and prescribing the "best" medicine. It encompasses a good humanely interaction. Patients and family members deserve a humanely interaction.
- Effective communication has been shown to improve not only patient satisfaction rates but also other health outcomes.
- Communication varies based on the gender, age, literacy, culture, and clinical settings
- Clinicians should identify potential barriers to communication in every encounter.
- The following are common barriers;
- Language or dialect
- Mental status or cognitive capacity

- Emotional/psychological distress
- Cultural differences
- Gender differences
- The environment: the examination room
- Steps to follow during clinical evaluation and communicating the client

1. Observe
    - Observe the patient as he/she enters the room for severity of illness and danger clinical signs to act accordingly.
2. Greet appropriately and establish rapport
    - Stand from your chair, call the patient by her or his name with appropriate title and give culturally appropriate greetings.
    - Establish a rapport: e.g. "Please sit down…. you look like tired", "Please, take a sit…. let me help you with your stick"
3. Give attention
    - Sit facing the patient, lean forward, establish eye contact and relax.
4. Listen
    - The golden "first minute" allows you to listen to the patient without interrupting, whatsoever.
    - Just give opening questions and listen:
        - ✓ "How have you been feeling?",
        - ✓ "What is bothering you? Tell me about it",
        - ✓ "Have you been feeling unwell? tell me about it"
5. Open ended questions initially
    - Ask about their chief complaints and their durations
    - Then ask more open-ended questions like "tell me more about

that" to explore about their complaints without interrupting.

6. Close ended questions when necessary
    - If needed ask guiding questions? E.g., did you have a travel history to such places? Have you ever experienced such symptoms?
    - Ask past history, drugs being taken, recent treatments and allergies
7. Do a complete physical examination
    - Focused but not limited to the complaints
8. Document your findings
9. Formulate a differential diagnosis and diagnosis
    - Give a brief explanation about the possible diagnosis.
10. Do relevant tests and imaging
    - Explain about the tests

- Communicating once the diagnosis is made, treatment planned and prognosis understood
    1. Briefly assess what the patient already knows: But don't push it hard, if they don't want to tell. See the examples below;
        - Example for educated urban dweller
        - "These days we get a lot of information from the media, the internet or communicating with health care workers, tell me what you know about this… and what really concerns you"
        - For uneducated a rural patient
        - "When we are sick, we discuss it with relatives, neighbors, other people with similar illnesses or elders. What have you heard about this…? tell me what you heard and what really concerns you"
        - Individuals vary on what they want to know

2. Be empathic
    - Empathy needs to be developed in every clinician's practice.
    - Without empathy one cannot understand the emotions of patients and communicate effectively.
    - Do not ignore or minimize patient's feelings.
3. Try to assess what the patient wants to know
    - Patients vary with the amount of information they want to receive.
    - Use direct and indirect cues to understand what the patient wants to know.
    - Encourage them to ask questions. There questions would give you clues to the level of understanding.
    - Ask questions: Do you like to know more about this? Anything else you want to know or ask?
4. Slow down
    - Speak slowly and deliberately.
    - Give pauses. It helps the client to think and understand.
5. Keep it simple
    - Use simple language and short sentences
6. Avoid medical jargon
7. Tell the truth
    - Be truthful
    - Do not minimize or soften the impact of a diagnosis or treatment. This type of information can be extremely misleading and create confusion, delay treatment and affect outcomes.
    - Inform the truth with all the potential solutions and words of support and partnership. "It is not something good that you

have this…... but we will do everything possible and I hope things will improve …...”

8. Be hopeful
    - While telling the truth in situations like advanced cancer, covey some hope.
    - The therapeutic options available.
    - Therapies that alleviate symptoms and give comfort.
9. Watch the patient’s body language
10. Be prepared for a reaction
    - Individuals vary in the way they react to stressful information.
    - Some could be non-emotional. This should not be taken as lack of worry or not understanding the severity of the problem.
    - Some could cry or show denial: let them express it, don’t interrupt but your body language should show signs of support.
    - Some could develop distrust and blame: do not react, do not let your emotions control you. It could be difficult to establish a good partnership with such patients.

- Don’t dos during clinical communication
    1. False reassurance
        - Clients get discouraged if most symptoms and feelings they tell are answered by reassuring them e.g., by saying “that is okay” “that is simple” “we all felt like that”.
        - They can feel their feelings are down-played or sometimes ridiculed.
    2. Rejecting
        - Avoid refusing patients ideas or belief without adequate explanation

3. Probing
    - Do not probe patients on issues they don't want to discuss
4. Asking "Why"
    - Asking "why" means the patient has to defend himself or herself. Rather, ask "how?".
5. Belittling patient's feelings or complaints
6. Judging patients or making stereotype comments
7. Interrupting conversation
    - Phone calls are the most common reasons.
    - Don't interrupt conversations to respond voice calls or distract your attention to watch your phone for texts or alerts.
    - If there are urgent issues, ask permission from the patient, tell the caller that you are with a patient while the patient listening and ask the caller "is there anything urgent" while the patient is listening.
    - You must show that the priority for you at that time is the patient.
8. Writing while having active discussion

FURTHER READING

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3. Iedema, R. and Manidis, M. Patient-Clinician Communication: An Overview of Relevant Research and Policy Literatures. Sydney: Australian Commission on Safety and Quality in Health Care and UTS Centre for Health Communication. ISBN: (2013). ISBN-10: 0988669501.

1.2. Chronic Care model: Provision of care for chronic diseases and the chronic care model

- Chronic diseases such as diabetes, hypertension, heat failure, cancer, chronic respiratory diseases, chronic kidney disease, and mental illnesses are major global public health problems.
- Some communicable diseases such as HIV and hepatitis B are chronic diseases that require follow up and treatment as in the non-communicable chronic diseases.
- The prevalence of chronic non-communicable diseases is rising in Ethiopia. The 2015 Ethiopian STEPS report on risk factors and prevalence of selected non-communicable diseases indicated that prevalence of hypertension is 16 % and impaired fasting blood sugar to be 5.4%.
- The management of chronic diseases is becoming a major component of primary care.
- In addition to clinical skills provision of chronic care requires a great deal of coordination, leadership and practice improvement.
- Most primary health care systems are designed for provision of acute care, which mainly involves evaluating and treating the disease once or a few times.
- Quality chronic care cannot be provided by a 15-minute or less interaction with health care provider which significantly varies from provider to provider.
- The care of patients with chronic diseases entails achieving certain targets, based on evidences. However, most patients with these diseases are either not getting the treatment at all or they are not treated to the recommended targets. This gap occurs due to several reasons but the most important ones are related to systems.
- Patients and their family members play important role in the care. Hence, they need to be educated about their illnesses and actively participate in their care. They are important in improving adherence to medications,

follow up and life style changes.

- The following are basic organizations that need to be in place for providing chronic care;
  1. Identify the chronic illnesses that can be followed in your institution.
  2. Select a team of health care workers that will be involved in this work.
  3. Identify an existing **space** which will be used for chronic illness follow up.
  4. Based on the standard treatment guidelines summarize the diagnostic and treatment protocol for each disease. Focus the following areas;
     I. How diagnosis is conformed? What additional clinical information is needed?
     II. The treatment protocol: Pharmacologic and non-pharmacologic.
     III. Follow up: Clinical &laboratory parameters to be followed and their frequency.
     IV. Clearly define optimal care: what are the targets to be achieved?
     V. The role of the patients and family members
     VI. Patient and family education materials
  5. Develop a recording keeping system
     - Do not allow every health care provider to record the way they like.
     - The format for follow up should be simple but includes the required relevant information.
  6. Create an appointment system
  7. Keep contact addresses of patients and families and have a tracing mechanism.
  8. Use the HIV care model as a template
- Once there is a chronic disease care provision service in your institution

continuous improvement in the quality of care is needed.

- There are different models used to improve the quality of chronic illness care provided in primary care.
- One of the most widely used models is the chronic care model (CCM). The chronic care model is a frame work of improving the quality of care. It has care six basic components.

1. Organizational support
2. Clinical information system
3. Delivery system design
4. Decision support
5. Self-management support
6. Community resources

Table 3.1: Components of the chronic care model

	Components	What is the component about and what we do?
1	Organizational support	Engagement and support from the leadership • The leadership plays important role in supporting changes, motivating staff, securing resources and removing barriers and providing motivation
2	Clinical information systems	Have a registry • Have a system or technology that provides clinicians with a comprehensive list and important details of patients with a given chronic illness, called registry. • It helps clinicians to track their patients' status and make decisions.
3	Delivery system design	Organizing visits and follow-ups • Use clear appointment plans • Have evidenced based recommendation for treatment • Ensure that there is a system that all patients receive the recommended treatment • Design an active follow up program as well: telephone visits

4	Decision support	Primary care providers need support and professional development • Guidelines will only be effectively implemented when provider get professional support. • Organize education for the staff • Create important in reminders in their rooms • Incorporate the summary of the guidelines in to flow charts, patient assessment tools • Get professional support from specialists.
5	Self-management support	Active patient and family involvement • Patient empowerment • Educate patients on self-management skills, setting their goals, have their own action plans and achieve their targets
	Community resources	The patient and the health care institutions are not enough • Supporting organizations small or big, charity, non-governmental, faith based, societies can provide useful support. • Create linkage to these organizations

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3. Curing the system: Stories of Change in Chronic Illness Care. Accelerating change today (A.C.T) for America's health, May 2002 National Coalition on Health Care and the Institute for Healthcare Improvement.
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1.3. General care for hospitalized patients

3.3.1 Intravenous (IV) fluid therapy in adults

BRIEF DESCRIPTION

- Intravenous (IV) fluids are one of the commonly prescribed interventions in clinical practice. They have been used for over a century
- Many clinicians take the decision of prescribing IV fluids very lightly or carelessly. However, IV fluids are drugs with benefits and risks.
- Inappropriate IV fluid prescription is associated with increased morbidity, mortality, and prolonged hospital stay.
- Understanding fluid-electrolyte homeostasis, conditions associated with fluid-electrolyte disturbance, the constituents of IV fluids, assessment of volume status of patients is important for clinicians who prescribe IV fluids.
- Total body water constitutes 60% of body weight in men and 50% in women. It is distributed in to the intracellular fluid (ICF) compartment (40% of body weight) and extracellular fluid (ECF) compartment (20% of body weight).
- The extracellular fluid is again divided in to interstitial (3/4 of ECF) and intravascular fluid (1/4 of ECF) compartment. A 70kg male adult will have the following;
    - Total body water = 70kg x 60% = 42liters
    - ICF= 70kg x 40%= 28liter
    - ECF= 70Kg x 20%= 14liter
    - Interstitial fluid = 14 x 3/4= 10.5
    - Intravascular (plasma) volume= 3.5 liter
- Under normal conditions the body maintains fluid (water) and electrolyte balance. The fluid input and output are balanced (equal) and the same for electrolytes.

FLUID BALANCE AND ASSESSMENT OF VOLUME STATUS

- Clinically fluid balance is defined as the difference between fluid intake (input) and fluid excreted (output). See the table below for components of fluid balance.

Table 3.2: Fluid balance components for adults under normal circumstances

Normal input	Volume in 24hour	Variability in healthy individuals
Water from oral fluid intake (average)	1500ml	Highly variable
Water contained in solid foods (average)	800ml	Variable
Water generated from metabolism	300ml	No significant variation
Normal output	**Volume in 24 hours**	**Variability in healthy individuals**
Urine	1500ml (Minimum 500ml)	Highly variable
Stool	200ml	Slightly variable
Sweating and respiratory loss	900ml	Highly variable ○ Loss from sweat can vary enormously from100ml to 2000ml) ○ Hyperventilation also increases fluid loss.
Insensible loss in adults for clinical purposes = 700ml/day (30 -40ml/hour) (ranges 600-900ml) *In febrile patients for every degree Celsius increase above 37, increase the insensible loss by 100 -150ml/day		

Fluid balance = Input# (oral + IV) – Output (Urine output + Insensible loss + Other losses*)

*__Other losses:__

- ✓ Drains/taps
- ✓ Diarrhea, vomiting, discharge
- ✓ Bleeding
- ✓ Loss from burn (depends on the surface area)

#Usually forgotten input: Fluid used to dilute IV medications or keep lines patent

1. **Negative fluid balance = LOSS OF FLUID**
2. **Positive fluid balance = GAIN OF FLUID**
3. **Zero fluid balance = NO LOSS OR NO GAIN (BALANCED)**

- Fluid balance is not easy to measure due to significant variations in the insensible loss, water gain from solid foods, and other factors.
- For hospitalized patients daily weight monitoring is reliable measure for fluid status.
- Incorporate daily weight monitoring as part of vital signs.
- In addition to fluid balance and weight monitoring volume status should be evaluated using clinical assessment tools.
- Good fluid status assessment = Daily Fluid balance + Daily weight monitoring + clinical assessment.
- Clinical tools used for assessing volume status are summarized as follows;

I. History indicating volume depletion

   - History of loss: Diarrhea, vomiting, polyuria, bleeding, burn
   - History of poor oral intake: Not able to take enough drinks or food
   - Thirst: usually excessive thirst

  - Decreased urine volume
  - Postural dizziness and palpitation

II. Physical examination indicating volume depletion

  - Vital signs: Low BP, postural drop in BP, tachycardia and tachypnea
  - Weight: daily weight monitoring is a very sensitive measurement.
  - Delayed capillary refill time: Press the pad (soft part) of the finger tips until it gets pale and watch how long it takes to return back. It is delayed if it is >2seconds
  - Skin and mucosa: dried oral mucosa, decreased skin turgor
  - Extremities: cold in state of shock

III. Physical examination indicating volume overload states

  - Weight gain: Daily weight measurement
  - Lungs: Lower lung zone crackles (also called crepitation or rales)
  - JVP and neck vessels: raised JVP and full neck veins
  - Liver: enlarged liver
  - Lower extremities: edema

IV. Investigation useful to make IV fluid therapy decision.

  - BUN and creatinine
  - Be cautious with IV fluids in patients with impaired kidney function as they might easily develop pulmonary edema
  - BUN to creatinine ration > 20 might suggest volume depletion but it never be used in obviously fluid overloaded (edematous patients)
  - Serum electrolytes
  - Sodium: crucial to decide the type of IV fluid
  - Potassium: important to decide on the addition of potassium.

INDICATIONS FOR IV FLUID THERAPY

- IV fluids are indicated when the fluid needs of an individual cannot be met with oral intake.
- The three main indications for IV fluid therapy are **resuscitation, replacement, routine maintenance (simply called maintenance)** 3R's. A 4th R is added in the IV fluid therapy to encourage removal when there is evidence of fluid overload in a patient.

Table 3.3: Indications for IV fluid therapy: 4R's

1. Resuscitation	• Rapid correction of shock using rapid boluses of IV fluids
2. Replacement	• Replace lost fluid until signs of hypovolemia improve • Continue replacement if there is ongoing loss
3. Routine maintenance	• Providing the daily fluid and electrolyte needs using IV fluid, when a patient cannot or is not allowed to take orally.
4. Removal	• When there are signs of fluid overload or excessive positive fluid balance, allow removal by stopping IV fluids or IV furosemide.

COMPOSITION AND AVAILABILITY OF IV FLUIDS IN ETHIOPIA

- Ideal IV fluid does not exist. It should also be known that the available IV fluids have significantly different composition.
- IV fluid prescription and administration require understanding the compositions of the IV fluids.
- The commonly available IV fluids in Ethiopia are the following;
  1. 0.9% saline (Normal saline or NS)
  2. Ringer's lactate (RL),
  3. 5%Dextrose in water (5%DW or D5W)
  4. 5%dextrose in normal saline (DNS or D_5NS).
- Unfortunately, all the available IV fluids come with similar 1000ml package. Other smaller packages like 500ml and 100ml are not available.

- Some important IV fluids and additives are not available in the Ethiopian market. This compromises choices and can result in using the wrong IV fluids or mixing existing fluids at the bedside, increasing the risk of infection and wrong volume proportions.
- We recommend having the following IV fluids and additives for clinical use in addition to the available ones;

  A. 0.45% saline (Half-strength normal saline, 1/2NS): for common use

  B. 0.45% saline with 5% dextrose: for common use

  C. 5% dextrose in Ringer's lactate: for common use

  D. Sodium bicarbonate: for common use

  E. 3% Saline (hypertonic saline): for specialized hospitals
- To improve ease and safety, we recommend availing at least: 500ml and 100ml volume packages.

Table 3.4: Compositions of common IV fluids

Fluid type	Na	Cl (mmol/l)	K (mmol/l)	Glucose (mmol/l)	Ca (mmol/l)	Buffer	Volume increase by 1L	Comment
Plasma (serum)	135-145	95-105	3.5-5.5	70-140 (mg/dl)	2.2-2.6	24-32	-	-
NS	154	154	0	0	0	0	250	Too much chlorine. Causes hyperchloremic metabolic acidosis
RL	130	109	4	0	1.35	28 lactate	250ml	A balanced crystalloid. Lactate is metabolized to bicarbonate.
5%DW	0	0	0	50 g/l	0	0	84	Electrolyte free water. Risk of hyponatremia.
DNS	154	154	0	50 g/l	0	0	300ml	
½ NS	77	77	0	0	0	0	125ml	Less chloride than NS
1/2NS with 5% dextrose	77	77	0	50g/l	0	0	200ml	

PRESCRIPTION AND ADMINISTRATION OF IV FLUIDS: BASED ON INDICATIONS

Resuscitation for hypovolemia

- Who needs IV fluid resuscitation, in state of hypovolemia?
    - Patients with severe hypovolemia
    - Severe hypovolemia = Cold extremities and delayed capillary refill >2seconds +/- other signs of hypovolemia (tachycardia, oliguria, dry buccal mucosa, dizziness)
    - Patients with Hypovolemic shock
    - Hypovolemic shock = severe hypovolemia (as above) + systolic BP (SBP) <90mmHg or mean arterial BP (Map) <65mg +/- change in mental status
- Which IV fluids to use for resuscitation?
    - Use either Ringer's lactate (RL) or Normal Saline (NS)
    - RL is preferred over NS, particularly if larger volumes continue to be required.
    - Never use 5%DW for resuscitation.
    - In case of hemorrhage, blood transfusion is preferred but as it takes time resuscitation should start with RL or NS.
- How much and how fast?
    - For adults: Give the first 1000ml (01liter) fast. Then reassess.
    - Assessment: BP, PR, mental status, capillary refill and extremities, urine output.
    - If the shock or signs of severe hypovolemia continue: Give 500ml bolus (over15 minutes) and reassess. If needed give another 500ml bolus.
    - After administering a total of 2000ml, revaluate. Look for ongoing loss and other causes of shock (sepsis, cardiogenic shock, cardiac tamponade, adrenal insufficiency).

  - If severe hypovolemia continues, give 200-300ml bolus 3-4 times; assess also for signs of fluid overload (particularly pulmonary crackles)

- When do we say resuscitation is completed and proceed to next step?
  - Minimum requirement: SBP >90mmHg or MAP>65mmHg, improved mental status, good urine output (>50ml/hour), improved capillary refill.
  - Shock might recur: with ongoing losses severe hypovolemia or shock might recur, hence, re-evaluation is needed.

Replacement

- What is replacement fluid?
  - IV fluid given to correct non-severe hypovolemia and ongoing losses.
  - It is given when there is hypovolemia but no need for renunciation or after resuscitation is completed.
- Which fluid is preferred?
  - The preferred fluid depends on the fluid lost and electrolyte abnormalities.
  - One must bear in mind that there is no ideal fluid; hence, monitoring of electrolytes is important.
  - The following serves as a guide for the preferred initial IV for common losses. Subsequent fluid should be decided based on serum electrolytes.

Table 3.5: Initial preferred fluid based on the clinical disorder

Loss/clinical disorder	Initial preferred fluid
1. Hemorrhage	Blood products
2. Diarrhea	RL
3. Vomiting	NS
4. Burn	RL
5. Intraoperative	RL
6. DKA/HHS	NS
7. Head injury/stroke	NS (do not add dextrose)

How much replacement fluid is given?

  - The volume of replacement fluid needed is variable depending on the degree of volume depletion, ongoing loss and urine output.
  - Give = estimated ongoing loss + urine output + 100ml/hour
  - If estimation is difficult give 150-200ml/hour (1liter over 06 hours for the first 12 -24hour) to achieve a urine output > 50ml/hr.
  - If there is any sign of fluid overload stop fluid. If there is worsening of hypotension give 200-300ml bolus and increase the rate of fluid administration.

- When to stop replacement?
  - When signs of hypovolemia are corrected and ongoing loss either stopped or can be corrected by oral fluid.
  - Do not leave IV fluid replacement order unrevised over 24 hours.
- Routine maintenance IV fluid
- Maintenance fluid therapy is needed when a patient is not able to or expected to eat or drink for a prolonged period of time e.g. Patient ordered to be NPO perioperatively, NPO ordered for resting the bowel, severe dysphagia, refractory vomiting.
- The goal of maintenance fluid therapy is to preserve water and electrolyte balance and to prevent starvation ketosis.
- What is the average fluid and electrolyte requirement for an adult, not taking oral fluids and food? Although it is variable, the following gives a good estimate
  - Water ~ 2000ml/day
  - Sodium ~ 1-2mmol/Kg/day
  - Potassium ~ 0.5-1mmol/kg/day (Half of the sodium). Hence for an average adult man (~70kg) the needs will the following in 24hr;
  - Water ~2000ml (25-30ml/kg/day)

  - Sodium ~ 70 -140mmol
  - Potassium ~ 35-70mmol
  - Glucose ~ 50-100g of glucose. This amount of glucose is just to prevent starvation ketosis and catabolism. This will not address the nutritional needs of an adult at all.
- What is the preferred IV fluid type for routine maintenance in adults?
  - The preferred fluid type: ½ strength (0.45%) NS with 5% dextrose + 20meq (01amouple of KCl) added in each liter. One liter(01bag) running for 12 hours.
  - The practical fluid type for maintenance: Because of the 0.45% NS is not available we recommend DNS (NS with 5% dextrose) + 20eq of KCl (01 ampoule added to it). DNS 1000ml + 20mmol of KCl (01ampoule) run every 12 hours.
  - Potential side effects: hyperchloremia, worsening of hypernatremia, hyperchloremic metabolic acidosis but as the volume of the maintenance fluid is low the risk is also low.
  - Alternative maintenance fluid: If DNS is not available, use the following as alternatives. We do not recommend routine use of the following as repeated puncture of the IV fluid bag for adding dextrose increases the risk of infection and increases cost significantly.
  - RL 1000ml + 20mmol of KCl (01ampoule) + 32g of glucose (80ml or 04 vials of 40% dextrose, each 20ml) run 12hrly OR
  - NS 1000ml + 20mmol of KCl (01ampoule) + 32g of glucose (80ml or 04 vials of 40% dextrose, each 20ml) run 12hrly
  - When to stop maintenance IV fluid?
  - As soon as the patient starts to take oral fluids or liquid diet.
- Complex medical problems where IV fluid therapy should be used cautiously. See the relevant topic in this guideline.
- Heart failure, impaired kidney function (AKI or CKD), nephritic or nephrotic syndrome: IV fluids should generally be avoided unless absolutely

needed. When used use low volumes with close monitoring.

- Cirrhosis and hepatic encephalopathy: Avoid RL and DW. Be cautious with NS or DNS.
- Poorly controlled diabetes: Avoid dextrose containing fluids
- Hyponatremia: Avoid D5W, RL. NS or DNS might be used.
- Hypernatremia: Avoid NS and DNS. Use D5W.

***Reminder**: The four D's of IV fluid therapy*.

1. Drug: IV fluids are drugs. They have indications, contraindications, benefits as well as adverse effects.
2. Dosing: Different indications (resuscitation, replacement or routine maintenance) have different dosing. Dose also varies depending on other factors.
3. Duration: Stop IV fluids when there are no more indications. Always ask" does this patient need IV fluids at this point in time)
4. De-escalation: When there are signs of fluid overload decrease or stop the IV fluid and consider IV diuretics if the fluid overload is severe.

FURTHER READING

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1.1.2. Intravenous lines: Care and Complications

- Intravenous (IV) lines or cannuale are one of the most commonly used devices in clinical practice.
- IV lines are commonly inserted to peripheral veins; however, in certain situation big IV lines might be needed to be inserted in to big central veins, these lines are called central lines.
- Peripheral IV lines are generally safe devices but if they are not inserted or cared appropriately, they can be associated with significant complications.
- Discussion on central lines is beyond the scope of this guideline, but guidance on the care and complications of peripheral IV lines were given below.

Insertion of peripheral IV lines (Cannulae)

Site selection

- Upper extremity
    - o Upper extremity veins are preferred.
    - o Try to avoid lower extremity veins due to high risk of thrombosis and thrombophlebitis.
- Non-dominant forearm
    - o Give preference to the non-dominant side (the left side in right-handed individuals and the vice versa).
- Start distally
    - o The distal posterior forearm veins are preferred; followed by veins of the dorsum of the hand.
    - o If the distal veins have been used repeatedly or fail, go to more proximal veins.
    - o Using proximal veins initially might result in extravasation and hematomas when distal veins are used later.
- Areas to avoid

  - Infected skin
  - Joints: in emergency situations (resuscitation) veins in the antecubital fossa (anterior elbow) can be used for about 24 hours.
  - Recently attempted site
  - Burnt skin or severe edema
  - Evidence of thrombophlebitis or repeatedly used veins
  - Arms in which there is hemodialysis arteriovenous (AV)fistula
  - In patients with CKD avoid the anterior forearm for future need of AV fistula

Insertion

- Consent, a verbal consent with appropriate explanation is adequate.
- Aseptic precautions.
- Hand hygiene.
  - Don't start insertion without having an alcohol-based hand rub with you.
  - The initial hand hygiene can be done using soap and water or alcohol-based hand rubs.
  - In between the procedure use alcohol-based hand rubs
  - After gloving, hand rubs should be applied on gloves as well.
- Skin disinfection
  - Wash the insertion site with soap and water if dirty before using antiseptics.
  - Preferred disinfectant: alcohol-chlorhexidine solution, 1-2% in ≥ 70% alcohol.
  - If not available: use either a 10% iodine in ≥ 70% alcohol solution or ≥ 70% alcohol solution

  - Apply the disinfectant in a circular motion to a wide area (~10cm long X 5cm wide)
  - Allow the antiseptic to dry.
- Non-touch technique
  - Do not touch part of the cannula to be inside the vein and the tip of the IV set.
- Don't shave (Clipping hair is preferred)
- Have a colleague to assist you: Only if possible

The insertion procedure

- Prepare equipment
  - Prepare all the necessary equipment, including normal saline for flushing.
- Select vein
  - Select vein, apply tourniquet to visualize it better and palpate it. Then, loosen or release the tourniquet.
- Disinfect the skin
  - Perform hand hygiene with alcohol-based hand rub, irrespective of gloving
  - Disinfect the insertion site as detailed above.
- Insert
  - Tighten the loosened tourniquet or reapply it.
  - Perform hand hygiene with alcohol-based hand rub.
  - Put on clean (non-sterile) gloves, if not applied at the beginning.
  - Insert the device: Using the direct or indirect method
    - Direct: Enter the skin over the vein directly at 30-40 degree.
    - Indirect: Enter the skin adjacent to the vein and direct it again to enter the side of the vein.

  - Advance the device slowly and steadily until you meet resistance.
  - Lower the needle to a 15 to 20 degree and slowly pierce the vein.
  - Observe flashback of blood. If you fail to see flashback, pull the catheter slightly back and observe.
  - If there no is flash back remove the catheter and try again
  - Tilt the needle lightly upward or pull back the needle slightly to advance the cannula. Push the cannula until fully inserted or you feel a resistance.
  - Withdraw the needle while applying a gentle pressure over the cannula to prevent bleeding.
  - Release tourniquet and remove the stylet.
- Flush with saline
  - Give saline push 2-4ml with a 10cc syringe or attach IV fluids.
  - A 10cc syringe is preferred as it produces lower pressure.
  - If the there is a resistance or there is a swelling remove the cannula immediately.
- Call a colleague
  - After three to four unsuccessful attempts at inform another colleague to attempts.
  - If there is any breach of aseptic technique, use a new cannula.
- Secure the cannula
  - Use sterile tape.

Table 3.6: Color coding of cannula base on size

Color	Size (gauge)	Flow rate (mL/min)
Orange	14	290
Gray	16	176
Green	18	76
Pink	20	54
Blue	22	31
Yellow	24	14

COMPLICATION DURING IV-LINE INSERTION

- Hematoma: When veins rupture or rarely when an artery is injured
- Arterial puncture or cannulation of an artery:
    - This serious complication tends to occur more in neonates and infants when the cannula is inserted in the antecubital fossa (elbow).
    - Suspect it when there is a bright red blood, pulsatile flow (comes-pause-comes-pause) with high pressure (pushing the syringe plunger).
    - When you suspect an arterial puncture/cannulation or when you have any doubt remove the cannula immediately, apply localized pressure with a single finger for 5-10 minutes and observe.
- Damage to nerves
- Vasovagal syncope (fainting)
    - Some patients are afraid of the sight of a needle or blood. It mainly occurs when the patient is in sitting position. If the patient is anxious or has previous history of syncope, do the insertion in supine position

CARE OF THE IV LINE (CANNULA)

- Observation (review)
    - During each shift (at the end of each shift) and every time when

  injections are given and infusion are changed
  - Observe for signs of phlebitis (see below)
  - Position
  - Infiltration
  - Bleeding
  - Soiling
- Inform and encourage patients or care givers to report when there is one of the followings:
  - Pain
  - Bleeding
  - Dislodgement
  - Flushing Intravenous fluid is completed
- Flushing
  - Before giving any injection or infusion
  - If not used, every 24 hours. Consider removing if not used for 48 hours.
  - During flushing use 10cc syringe to decrease pressure
  - Flush with normal saline 3-5 ml in pulsatile way (push-stop-push)
- Re-site (remove and change to another site)
  - When there are signs of phlebitis
  - The IV site is not functional
  - If there is infiltration or extravasation
  - If the IV site stayed for more than 4 days and it is still necessary. Needed and functional IV lines without signs of phlebitis may be kept for more than 5 days, if the patient has difficult vein or in children.
  - IV line inserted at referring health institutions need to be changed (re-

sited) if there is no clear indication when they were inserted.

  - IV lines inserted on the neck (external jugular) should be changed as soon as other peripheral veins are accessed.

- Removal
  - Remove any IV line which is not needed.
- Changing IV set (administration set)
  - Change immediately: after giving chemotherapy or blood products (blood products need a different set provided by the blood bank service)
  - Change in 24hour: continuous infusion of heparin or lipid containing parenteral nutrition
  - Change when IV site is changed: Change the IV set every time there a new cannula inserted.
  - Do not change when not indicated: Frequent changes in IV sets without indications increases the risk of infection
- Medication labeling
  - All bags or bottles of intravenous fluids or medications should be labeled, containing the following information;
  - Name of the patient
  - Date and time of start
  - Rate of infusion
  - Nurse's (any other any care professional doing it) name and sign
- Hand hygiene
  - All health care workers should perform hand hygiene using alcohol-based hand rubs (>70% alcohol) or wash with soap and water in the following circumstance;
  - Insertion or removal (before putting gloves), dressing change, drawing blood, or before

- Before manipulation or changing dressing
- Before opening the IV set (administration set)
- During preparation of medications for IV administration

COMPLICATION ASSOCIATED WITH PERIPHERAL IV LINES

- Phlebitis: Inflammation of the vein due to either infection, chemical irritation caused by the medications given or mechanically induced by the cannula itself.
- IV line (catheter) associated blood stream infection: when microorganisms enter in to the blood stream via the IV line.
- Infiltration: when a non-vesicant solution ruptures in to the tissue surrounding the vein. This occurs when tip of catheter slips out of the vein or passes through the wall of the vein, or as the vein stretches it allows fluid to pass into the surrounding tissue.
- Extravasation: occurs when a vesicant drug or fluid infiltrates into the tissue surrounding the venipuncture site.
- Thrombosis: When a clot forms in with within the lumen of the cannula or the vein where the cannula is inserted.
- Dislodgement: a cannula can dislodge if it is not properly fixed.

Signs of phlebitis

- Early signs
    - Swelling
    - Redness
    - Hotness
    - Pain: along the path of the cannula
- Late signs
    - Fever
    - Cord like vein (hard to palpate)
    - Pussy discharge

FURTHER READING

1. Australia, Queensland Government Department of Health Centre for Healthcare Related Infection Surveillance and Prevention & Tuberculosis Control Guideline for Peripheral Intravenous Catheters [PIVC] *Version 2 – March 2013.* *https://www.health.qld.gov.au/__data/assets/pdf_file/0025/444490/icare-pivc-guideline*
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3.3.3. Pressure (Bed sore) prevention and management

- A pressure sore/ulcer (bed sore) is a localized injury to the skin and the underlying tissue resulting from unrelieved pressure.
- The sore arises as a result of the soft tissue compression between a bony prominence and external structures (e.g., bed, stretcher or wheelchair).

- Pressure sores pose a huge burden on patients, families, and health care systems.
- The rate of development of pressures sores in hospital wards is one of the key indicators of the quality of nursing care.
- Prevention and management of pressure sores is a fundamental aspect of the care of hospitalized patients.

Who is at high risk for pressure sore?

- The risk factors for pressure sore can be related to the patient (intrinsic) or the external environment. See the table below.

Table 3.7: Risk factors for pressure sore

I. PATIENT RELATED (INTRINSIC) RISK FACTORS		
No.	**Risk factors**	**Typical examples**
	Decreased mobility	Paralysis from any cause, coma or prolonged sedation, fracture
	Comorbidities	Peripheral arterial disease, decreased pain sensation, malignancy, diabetes mellitus, dementia, heart failure
	Poor nutritional status	Anorexia or cachexia from chronic illness, catabolism from acute illnesses, dehydration
	Ageing skin	
II. EXTERNAL (EXTRINSIC RISK FACTORS)		
No.	**Risk factors**	**Typical examples**
	Pressure from hard surfaces	Beds, wheelchair or stretcher
	Moisture	Urinary or fecal incontinence, excessive sweating, discharges
	Friction or shear	From patient inability to move and involuntary muscle movements

ASSESSING THE RISK OF PRESSURE SORE IN INDIVIDUAL PATIENTS

- There are a few validated score (scales) to assess the risk of pressure sores in individual patients.
- None of the scoring tools completely replace clinical evaluation; however, they provide objective, reproducible and comprehensive guide.
- One of the commonly used scales, BRADEN SCALE is provided in the table below.
- The BRADEN scale needs to be completed at the time of admission and reassessment needs to be depending on the patient's clinical condition. In patients who are clinically deteriorating, the score should be revised more frequently.

Table 3.8: BRADEN SCALE For predicating pressure sore risk

Name of the patient: ________________________ Date of assessment: _________________________			Hospital no. __________ Name of the HCW: _____		
Risk factor	Score				
	1	2	3	4	patient's score
1. Sensory perception (Ability to respond to pressure related discomfort)	Completely absent	very limited	Slightly limited	No impairment	_____
2. Moisture (Degree to which the skin is exposed to moisture)	Constantly moist	Often moist	occasionally moist	Rarely moist	_____
3. Activity (Degree to which patient moves)	Bed bound	Chair bound	Walks occasionally	Walks frequently	_____
4. Nutrition (Usual food intake pattern)	Very poor	Probably inadequate	Adequate	Excellent	_____
5. Friction and shear (Ability to move on bed or chair)	Requires moderate to maximum assistance	Moves but with minimum assistance	Moves independently	-	_____
Total score of the patient					_____
Interpretation: the lower the total score, the higher the risk of pressure sore. Total score < 12 = high risk 13 – 14 = Moderate risk 15 – 18 = Low risk					

Evaluating the patient for the presence of pressure sores

- Inspect the skin every time the patient is repositioned
- All skin areas from head to toe need to inspected quickly, focusing on bony prominences: Sacrum, Ischial tuberosity, greater trochanters of the femurs, heels
- Look for the presence of visible ulcer, erythema, swelling, induration (hardness), hotness or coldness.
- If there is visible change or ulcer, describe and categorize the lesion.
- Ulcer: Location, size (width X length in cm), stage, discharge (exudate)

Table 3.9: NPUAP/EPUAP pressure ulcer classification system

Stage / category	Description
I. Non-blanchable Erythema	▪ Intact skin with non-blanchable redness of a localized area usually over a bony prominence ▪ The area may be painful, firm, soft, warmer or cooler. ▪ It may be difficult to detect
II. Partial Thickness Skin Loss	▪ Shallow, open ulcer with a red/pink wound bed. ▪ May also present as an intact or ruptured blister.
III. Full Thickness Skin Loss	▪ Full thickness skin loss, subcutaneous fat may be visible. ▪ Bone, tendon or muscle are not exposed.
IV. Full Thickness Tissue Loss	▪ Full thickness tissue loss with exposed bone, tendon or muscle. The exposed tendon/bone is visible or palpable. ▪ Slough or eschar may be present on some parts of the wound bed.
V. Unstageable: Depth Unknown	▪ Full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed. ▪ Stable (dry, adherent, intact without erythema or fluctuance) eschar on the heels should not be removed.

Preventive care for pressure sores

- All high-risk patients should be provided with preventive care.
- Skin care
    - Keeping the skin clean.
    - Cleanse the skin promptly after episodes of incontinence.
    - Use high absorbency incontinence products.
    - Avoid vigorously massaging or rubbing the skin.
    - Use emollients (e.g., paraffin, Vaseline, petrolatum) in dry skin and old individuals
- Positioning and repositioning
    - Reposition frequency depends on the individual conditions. It should be prescribed clearly.
    - Determine repositioning frequency based on the individual's level of mobility, general condition, comfort, and pain.
    - For patients who can't move at all, repositioning is typically needed every 2 hours.
    - Have a reminder strategy to adhere to the repositioning schedule.
    - Use 300 tilt position (Tilt the pelvis with pillow under the buttock and a pillow in between the legs). See the picture below.
    - Position in the right, back, left side +/- prone alternatively. Use prone position if the patient condition allows.
    - In hemodynamically unstable patients repositioning should be down slowly and with close observation.
    - Avoid positioning on bony prominences, erythematous skin, an already formed ulcer or medical devices (tubes, drains or foreign bodies).
    - Avoid dragging; rather use lifting e.g., using bed sheets.

  - To decrease sliding down avoid positioning patients in semi-recumbent positions; unless medically contraindicated e.g.in patients with heart failure.
  - In patients with heart failure or other fluid overload states, keeping patients in semi-recumbent or sitting (900) is absolutely needed.
  - Ensure the heels are off the surface. Elevate the heels using a pillow or other cushions.
  - Offload the heel completely and distribute the weight of the leg along the calf without placing pressure on the Achilles tendon.
  - Do not leave a patient on a bed pan for a long period of time.

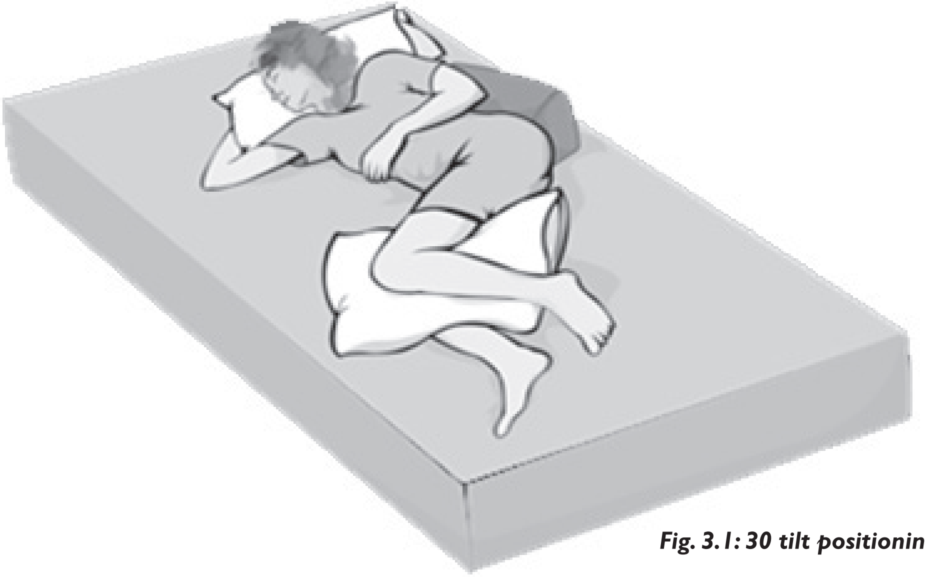

Fig. 3.1: 30 tilt positioning

- Nutrition and hydration
  - Evaluate the nutritional and hydration status of patients. Treat malnutrition
  - Most hospitalized patients need high calories and high protein diet.
  - Encourage patients to take foods rich in vitamins and minerals; if not

possible, provide multivitamin and mineral supplements.

  - Make sure patients are well hydrated.
- Keep sleeping and sitting surfaces clean and dry
  - Keep bed sheets clean and dry. Change bed sheets promptly when they get wet or soiled.
  - Make sure mattresses are comfortable and distribute weight evenly.
- Regularly inspect the skin
  - See above on evaluating for the presence of pressure sores
- Managing a pressures sore.
  - Management of a pressure sore depends on the stage, the presence or absence of necrotic tissue, and the presence or absence of infection.
- Pain control
- Cleansing the wound: stage II and above
  - Cleanse the wound every time dressing is done
  - Use normal saline for cleansing.
  - Do not use hydrogen peroxide for any degree of pressures sore. Hydrogen peroxide is too toxic for tissue even at low concentrations.
- Dressing; Stage II and above
  - Apply dressing to open pressure sores (stage II and above).
  - Moist dressing is preferable. The most practical one in the Ethiopian setting is saline moist gauze dressing.
  - Use a single gauze to cover deep ulcer.
    - The frequency of changing the dressing depends on the amount exudate. Initially more frequent (twice daily to daily), subsequently the frequency of dressing might be reduced, depending on the healing.

- Debridement: Stage III and IV
    - Devitalized (dead or necrotic tissue) should be debrided.
    - There are two types of debridement: Sharp (surgical) or non-sharp (non-surgical).
    - Sharp (surgical debridement): stage III or IV ulcer with necrotic tissue and features of cellulitis, abscess, crepitus or sepsis needs urgent sharp debridement.
    - Non-sharp debridement: Stage III or IV ulcer with non-adherent necrotic tissue and no urgent indication. The most practical approach in Ethiopian setting is mechanical debridement before each dressing session.
    - Do not debride dry eschar (dark or brown) on the heel or ischemic limbs.
- Systemic antibiotics
    - Use of systemic antibiotics is indicated when there is evidence of spreading infection. The following are the indications;
        - Sepsis suspected to originate from infected wound
        - Cellulitis: hot, red, swollen, and tender surrounding tissue
        - Osteomyelitis: clinical and radiologic evidence
    - Infections of pressure ulcers are typically polymicrobial. The most commonly isolated organisms include staphylococci and streptococci as well as enterococci, Enterobacter, Proteus, and anaerobes
    - Antibiotics choice should be driven by local sensitivity data of these organisms when there are indications (see the relevant chapter for antibiotic choices)
- Topical antibiotics
    - Topical antibiotics are not indicated in the routine care of pressure sores.

  - Topical antibiotics might be considered when there in non-healing ulcers with no overt infection but a possibility of bio-film is considered.
- Evaluation of healing
  - Assess pressure sore for healing: decreasing wound size, decreasing exudate, clean wound bed, and granulation.
  - If the wound does not show evidence of healing in two weeks' time with wound care, alleviation of pressure and nutritional support, look for evidence of infection (superficial or deep) or non-debrided necrotic tissue.
- Surgical consultation**:** Consult surgical team when the following are evident
  - Sepsis suspected form the wound
  - Cellulitis advancing from the pressure ulcer
  - Crepitus
  - Persistent malodor
  - Fluctuant lesion
  - Crepitus

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Pressure ulcers: prevention and management. Published: 23 April 2014. www.nice.org.uk/guidance/cg179

3.3.4 Stress ulcer prophylaxis and treatment

- Stress ulcers area gastric ulcers which occur in critically sick patients in ICUs or patients with burn, and sever trauma.
- Stress ulcer commonly occurs in the fundus and body of the stomach but can also occur in other parts of the stomach the duodenum or esophagus.
- A clinically important stress ulcer bleeding is defined us an upper GI bleeding in critically sick patients resulting hemodynamic deterioration or requiring blood transfusion.
- The two major risk factors for clinically important stress ulcer bleeding are being on a mechanical ventilator for more than 48 hours and the presence of coagulopathy.
- Overt stress ulcer bleeding in ICU patients is associated with increased mortality.
- The clinical manifestations of a bleeding stress ulcer are: hematemesis (coffee ground or frank red blood in the NG tube aspiration or vomiting), melena, progressive drop in hemoglobin.
- All patients admitted to ICU, patients with severe burn and, trauma need evaluation for possible stress ulcer prophylaxis.
- Indication for providing stress ulcer prophylaxis
    - o Mechanical ventilation for >48 hours.
    - o Coagulopathy: platelet count <50,000 per m^3 or INR >1.5, or PTT >2 times the upper limit of normal.
    - o History of upper GI bleeding or confirmed peptic ulcer disease in the past year.
    - o Traumatic brain or spinal cord injury
    - o Severe burn
    - o Two or more of the following minor criteria: severe sepsis/septic shock, ICU stay > 1week, or glucocorticoid therapy (>250 mg hydrocortisone or the equivalent)

- Which agents to use for prophylaxis?
- Either a proton pump inhibitor (PPI) or a histamine-2 (H2) blocker can be used.
- Route: oral (NG tube) or IV route can be used.
- Dose:
  - **Omeprazole** 20 - 40mg, PO (via NG tube) or IV once daily

    OR
  - **Cimetidine** 400mg, PO (via NG-tube) BID to TID or 200mg IV, BID to TID
- Duration: the prophylaxis should only be given as long as the risk factors are there. It should be discontinued when there are no risk factors.
- **Potential harms of providing stress ulcer prophylaxis**
  - Suppression of gastric acid secretion in critically ill patients is associated with increased risk of nosocomial pneumonia and Clostridium difficile infection (CDI).
- Prophylaxis should only be provided for high-risk patients (see above).

> Stress ulcer prophylaxis is not indicated in non-ICU hospitalized patients and ICU patients without risks.

MANAGEMENT OF A BLEEDING STRESS ULCER

- Resuscitation
  - Patients with hemodynamic compromise should be resuscitated with crystalloids promptly. It is good to warm the crystalloids to avoid hypothermic coagulopathy.
  - Whole blood should be prepared in the meantime and transfusion should be the main stay of resuscitation once it is made available
- Correction of coagulopathy
  - If INR > 1.5: Give fresh frozen plasma (10-15ml/kg) which is 3 -4 bags,

then follow if the coagulopathy is corrected or not.

  - o If platelet is <50,000 or the patient has been on Aspirin or Clopidogrel: 06 units of platelets and check if the bleeding is corrected

- Nasogastric (NG) tube placement
  - o NG tube should be inserted in all patients with stress ulcer bleeding for decompression +/- lavage.
- Proton pump inhibitor, intravenous route
  - o Omeprazole 80mg IV loading followed by 40mg IV BID: preferred for cost effectiveness.

    OR

  - o Esomeprazole 80mg IV loading followed by 40mg IV BID

    OR

  - o Pantoprazole 80mg IV loading followed by 40mg IV BID
- Alternative: If Intravenous PPIs are not available use oral Proton pump inhibitors with similar doses as in the IV.
- Endoscopy
  - o Endoscopy is indicated for all patients with suspected stress ulcer bleeding for both diagnostic and therapeutic purposes.
- Surgery
  - o Surgery is indicated in patients with refractory bleeding despite conservative therapy or if there is evidence of perforation

FURTHER READING

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3.3.5 Hospital acquired infection prevention

- See chapter II on antimicrobial resistance and its containment, topic 2.3 hospital acquired infection prevention.

3.3.6 Surgical wound infection: prevention and management

- Surgical site infections (SSIs) are infections which occur at or near a surgical incision site or the organ operated or the space left after surgery, within 30 days of the procedure or 90 days if a prosthetic material is implanted.
- SSIs can be superficial, deep, organ/space specific;
  - Superficial infection: involving the skin or subcutaneous tissue of the incision.
  - Deep infection: involving the deep soft tissue of the incision (fascial & muscle layers)
  - Organ/space infection: involving any part of the organs or spaces that was manipulated during surgery.
- SSIs are common sources of hospital acquired infection with an associated increase in morbidity and mortality, hospital stay, and increased cost of care.
- Nearly half of SSIs are preventable by applying good clinical practice.
- SSIs arise from interaction of several risk factors; including the degree of contamination of the site at the time of the surgery, overall health of the patient, use of appropriate antimicrobial prophylaxis, and the technique of the surgeon.
- Some of the patient related risk factors are smoking, obesity, diabetes, malnutrition, use of steroids and other immunosuppressive medications, old age, and anemia.

- Surgical wounds are classified based the degree of contamination of the surgical wound at the time of the operation. (See the table below)

Table 3.10: Wound class as it applies to surgical wound

Wound class	Description
1. Clean	▪ An incision in which no inflammation is encountered during the procedure, without a break in sterile technique. and ▪ The respiratory, alimentary, genital, or urinary tracts are not entered.
2. Clean-contaminated	▪ An incision through which the respiratory, alimentary, or genitourinary tract is entered under controlled conditions but with no contamination encountered.
3. Contaminated	▪ An operation in which there is a major break in sterile technique or gross spillage from the gastrointestinal tract. or ▪ An incision in which acute, non-purulent inflammation is encountered. or ▪ Open traumatic wounds that are >12 - 24 hours old.
4. Dirty or infected	▪ An operation in which the viscera are perforated or when acute inflammation with pus is encountered. or ▪ Traumatic wounds in which treatment is delayed, there is fecal contamination, or devitalized tissue.

- Wound healing can occur with either primary or as secondary intention.
- Healing by primary intention occurs when a wound has been sutured after an operation and heals leaving a minimal, cosmetically acceptable scar.
- Healing by secondary intention occurs when a wound is deliberately left open at the end of an operation because of excessive bacterial contamination or when there is a devitalized tissue.
- Wound healing by secondary intention may be sutured within a few days (delayed primary closure), or much later when the wound is clean and granulating (secondary closure), or left to complete healing naturally without suturing.
- Prevention of surgical site infections
- Several interventions in perioperative period have been shown to reduce the risk of surgical site infections; they are summarized in the table below.

Table 3.9: Preventive interventions to decrease surgical site infection

Preoperative interventions		
Intervention	Additional information	Responsible body
• Patients' baths or showers before surgery		• Patient and surgical ward team
• Mechanical bowel preparation for elective colorectal surgeries		• Surgical ward team
• Do not remove hair. If absolutely necessary, do not shave, rather use clippers		• Surgical team
• Give prophylactic IV antibiotics 60-120 minutes before incision when there is indication. o Consider the half-life of the antibiotic and the time needed for infusion to achieve the high tissue concentration during incision o In cesarean delivery give the prophylactic antibiotic before skin incision.	• Indications o Clean-contaminated o Contaminated procedures. o Dirty or infected wounds require therapeutic, not prophylactic, antibiotics	• Anesthetist or surgical team
• Scrubbing (proper hand hygiene)		• Surgical team
• Do not discontinue immunosuppressives		>>
Intraoperative		
• Use sterile drapes and surgical gloves		• Surgeons
• Use alcohol-based solutions for skin preparation	• Alcohol based chlorhexidine solutions are preferred. • If chlorhexidine solutions are not, use alcohol-based povidone-iodine solution. • If it is not also available aqueous povidone-iodine solution	• Surgeons + pharmacy (procurement)

• Maintain adequate tissue perfusion and oxygenation. • Administer 80% Fio2 and keep SPO2 >95%		• Anesthetist
• Avoid hypothermia	• Use available warming mechanisms	• Surgical team
• Maintain asepsis and discipline in the operating room		
Post operatively		
• Administer 80% FiO2 in the first 2-4 hours postoperatively		• Anesthetist and surgical ward team
• Do not administer additional prophylactic antibiotics in the postoperative period, in clean and clean-contaminated wounds, even with the presence of a drain		Surgical team
• Wound care	• Evaluate the wound using non-touch technique • Cleanse and dress the wound	• Surgical ward team
• Glycemic targets: keep blood sugar < 200mg/dl all the time in both diabetic and non-diabetic patients		• Ward team and medical department

rates

- How to select antibiotics for prophylaxis?
- The commonest organisms causing surgical site infection in clean procedures are streptococcal species, Staphylococcus aureus, and coagulase negative staphylococci.
- In clean-contaminated procedures in addition to the above, gram negative rods and enterococci predominate.
- In a surgical procedure involving a viscus, the organisms involved reflect the flora and it is polymicrobial.
- The prophylactic antibiotic choice depends on the procedure type as mentioned above and the local antimicrobial sensitivity.
- Intravenous route is preferred.
- Evaluation of surgical wounds
- Surgical wounds need to be evaluated regularly using a non-touch technique, assess the bed, edge, size, presence of exudate, presence of dead tissue (eschar or slough), tunneling and categorize the wound condition as follows:
    - New epithelialized: wound completely covered with epithelium, no exudate, and no signs of infection.
    - Fully granulating: wound bed filled with granulation tissue to the level of the surrounding skin, no dead space or devitalized tissue, no signs of infection.
    - Early/partial granulation: > 25% of wound bed covered with granulation tissue, < 25% covered with devitalized tissue (eschar and/or slough), no signs or symptoms of infection and wound edges open.
    - Not healing: wound with > 25% avascular tissue (eschar and/or slough) or the presence of sign of infection or clean but non-granulating wound bed or closed/hyperkeratotic wound edges.
- Wound cleaning and dressing

- Clean wounds healing primary intention need little intervention other than protection by clean dressing and regular observation.
    - Cleansing will be required if any foreign material, debris, exudate or devitalized tissue is observed.
    - Clean with normal saline.
    - Showering can be allowed after 48 hours, unless the surgeon has a specific recommendation.
- Wounds healing by secondary intention or with dehiscence:
    - Need cleansing with normal saline with the aim of removing foreign materials, debris, and lose dead tissue.
    - Debridement: the need and the type (sharp vs. non-sharp) should be decided by the surgeon depending on the extent of adherent devitalized tissue.
    - Loculated abscess should be opened and drained
- Treatment of surgical wound infections
- Localized infection with no signs of cellulitis or systemic symptoms like fever need wound cleansing and debridement (if needed) only. No need of antibiotics.
- Fever: fever < 48 hours from surgery is unlikely from wound infection, >96 hours (04days) it is likely to be wound infection among other causes, in between 48-96hours it is a possibility.
    - Explore the wound: examine the wound, remove sutures, drain any collection and take samples for culture.
    - Start systemic antibiotics depending on sensitivity data
    - Infections above the waste (the diaphragm):
        A. Coverage of *Staphylococcus aureus* with either cloxacillin or a first- or second-generation cephalosporin or Clindamycin.
        B. If high rates of methicillin resistant *Staphylococcus aureus*: cover

methicillin resistant staphylococcus with vancomycin.

C. If the patient has other features of sepsis: start vancomycin.

- o Infections below the waist (the diaphragm): coverage of gram negatives, anaerobes, and gram positives needed.

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4. Surgical site infections: prevention and treatment. National Institute for Health and Care Excellence (NICE) guideline (NG125). 11 April 2019. www.nice.org.uk/guidance/ng125

3.3.7. Urinary bladder catheter care

- Urinary bladder catheterization is a common procedure done in both in-patient and out-patient settings.
- Although it appears to be a simple and straightforward procedure, it is associated with significant complications.
- The most common complication associated with indwelling urinary is urinary tract infection called catheter associated urinary tract infection (CAUTI) and the sepsis associated with it.
- Other complications include urethral trauma/erosion/perforation, bladder perforation and fistula, retention of balloon fragments, encrustation

(deposition of mineral salts resulting in obstruction) and bladder stone formation.

- External ("condom") catheters in males can cause pressure associated ulceration of the skin, pigment changes, and in prolonged applications the ring of the catheter can cause ischemia and necrosis of the penis.
- Rate of CAUTI is considered one quality measure of hospitals.

PRINCIPLES OF URINARY BLADDER CARE

- Catheterize when only absolutely needed.
- Keep the catheter if and only if the patient still needs it.
- Apply aseptic precautions and rigorous infection prevention practice.
- Provision of consent, ensuring privacy, dignity to the patient.

APPROPRIATE INDICATIONS FOR INDWELLING URINARY CATHETER (FOLEY) INSERTION*

(Modified from The Ann Arbor Criteria for Appropriate Urinary Catheter Use. *Ann Intern Med.* 2015;162: S1-S34. Reference number 2.)

- Acute urinary retention due to non-traumatic causes. E.g., BPH and medications which cause bladder outlet obstruction.
- Chronic urinary retention with bladder outlet obstruction.
- Stage III or IV pressure ulcers that cannot be kept clear of urinary incontinence other urinary management strategies.
- Urinary incontinence in patients for whom it is found difficult to provide skin care despite other urinary management strategies.
- Hourly monitoring of urine volume needed for fluid/vasopressor decision or as part of close hemodynamic follow up in critically ill patients.
- During surgery: to follow volume status and prevent bladder over-distention.

- After specific surgeries of the genitourinary tract or adjacent structures (i.e. urologic, gynecologic, colorectal surgery).
- For preventing severe pain caused by movement to urinate e.g., acute fracture
- In the management of gross hematuria with clots for the purpose of irrigation.
- Improving the comfort of a patient receiving end of life care, if catheter insertion addresses the patient's and family's goals.
- Contraindications to indwelling urinary catheter
- The only absolute contraindication to insert a Foley catheter is urethral injury, commonly associated with pelvic trauma.
- Gross hematuria or the presence of blood at the urethral meatus in a patient with pelvic trauma should be considered as possible urethral trauma.
- Relative contraindication includes systemic bleeding, urethral surgery, the presence of false passages, and urethral surgery.
- Inappropriate use of indwelling urinary catheters
- Urinary incontinence when skin care and other cares can keep the patient dry; including patients with dermatitis or grade I-II pressure ulcers.
- Routine use in ICU without the above-mentioned indication.
- Urine sample collection for sterile or non-sterile specimens, if possible, by other collection strategies.

APPROPRIATE INDICATIONS FOR CONDOM (EXTERNAL) CATHETER USE

Indications for external catheter use are similar to indwelling catheter except the fact that it should not be used for patients with urinary retention or management of gross hematuria with clots.

Indwelling urinary catheter selection, preparation, and insertion

- Clinician's order
  - Urinary catheterization should be performed up on the order of a clinician.
- Consent
  - Verbal consent should be received.
  - During consent adequate explanation on the need to catheterize, about the insertion procedure, expected duration, the potential discomfort, and possible complications.
- Privacy and dignity
  - The procedure should be done in private procedure rooms or using appropriate shield.
  - The procedure should be done in a dignifying manner.
- Catheter size
  - Length: The standard-length Foley catheter (40-44 cm) can be used in hospitalized women and women.
  - In ambulatory women shorter length catheters (23-26cm) are preferred, if available.
  - Short length catheter should never be used in men as it causes damage to the prostatic urethra.
  - Charriere (Fr) Size: The smallest size that provides adequate drainage should be used.
    - Females= 14 or 16
    - Male = 16 or 18
  - Balloon size: A 5cm balloon size should be used for routine catheterization. Check the manufacturer's recommendation on the balloon size.
- The procedure

  - Needed materials: appropriate size catheter, 2 pairs of sterile gloves, cleansing agent (normal saline), lubricating gel (sterile, closed), syringe filled with water for injection, drainage bag, bed protection (disposable pad), and alcohol-based hand rub.
  - See the table below for detailed description of the procedure.
- Urinary catheter and drainage system care
- Avoid kinking of the catheter or collecting tube.
- Keep the urine collecting bag below the level of the bladder at all times.
- Do not rest the bag on the floor.
- Empty the urine bag regularly. Do not keep it until it is full, empty when it about two-third fill.
- Avoid contact of the drainage plug with the collecting container.
- Unless obstruction is anticipated as in bleeding after prostatic or bladder surgery irrigation should be avoided.
- Do not clean the periurethral area with antiseptics in an attempt to prevent infection (CAUTI). Routine hygiene such as cleansing the meatus area during bathing is appropriate.
- Do not use topical or systemic antibiotics in an attempt to prevent CAUTI
- Do not change catheter at fixed regular intervals. It should be when clinical indications such as, obstruction, infection, or when the closed system is compromised.
- Urine sample collection: For urinalysis and culture, aspirate urine using sterile adaptor or after clamping collect the urine directly in to test tube. For large volumes of urine (e.g., 24-hour urine for protein or electrolytes) can be obtained from the urine bag.

Table 3.12: Indwelling urinary catheter insertion procedure

1. Positioning, preparation of equipment and sterile filed	
• Explain & discuss procedure with patient. Receive verbal consent.	
• Ensure good light source is available	
• Perform hand hygiene (water and soap or alcohol-based hand rub)	
• Inform or assist or remove patient's lower garments in respectful manner.	
• Assist into supine position with legs bent and hips flexed.	
• Place protection pad on the bed. Cover patient's body.	
• Prepare work area with required equipment.	
• Open out sterile dressing pack using an aseptic technique.	
• Pour normal saline into container. Open gloves, gel, catheter	
• Create a sterile field. Arrange the sterile drape under patient's buttocks and thighs.	
• Perform hand hygiene again and put on sterile gloves	
2. Insertion of the catheter	
Female	Male
• Using sterile swabs, separate the labia minora so that the urethral meatus is visible. • Using sterile swabs, cleanse around the urethral orifice with saline using single downward strokes. • Apply lubricating gel to the urethral office or at the tip of the catheter • Remove and dispose of the first pair of gloves • Perform hand hygiene • Apply 2nd pair of sterile gloves • Position a sterile container to catch urine • Open the inner cover of the catheter and expose 10cm of catheter • Introduce the tip of the catheter into the urethral orifice in an upward (superiorly) then backward (posteriorly) direction. • Advance the catheter until 5 - 6 cm has been inserted. When urine is present advance the catheter 6–8 cm.	• Hold the penis with a sterile swab, retract the Foreskin (if present) • Clean the glans and urethral orifice with saline. • Hold the penis with a sterile swab below the glans, raise it until it is almost totally extended. • Maintain this position until the catheter is inserted and urine flows. • Insert catheter gently into the urethral orifice, slowly advance the catheter up the urethra for 15-25cm. • If resistance is felt at the external sphincter slightly increase the traction on the penis and apply gentle steady pressure on the catheter. Ask the patient to strain slightly or cough. • Once urine flows, advance the catheter almost to its bifurcation. • Reduce or replace the foreskin

3. Fixing and connecting the catheter
• Inflate the catheter balloon slowly with sterile water 5cm or as per the manufacturer's recommendation.
• Observe patient for signs of pain and distress.
• Withdraw catheter gently until resistance is felt to ensure the catheter balloon is inflated.
• Attach the catheter to a sterile closed drainage system
• Ensure vulva area or the glans is clean and dry
• Measure amount of urine drained

(*Adapted from Adult Catheterisation and Catheter Care Guidelines. NHS Grampian Corporate.* NHSG/ACCCG/GUI/001)

Further reading

1. Carolyn V. Gould; Craig A. Umscheid; Rajender K. Agarwal et al. GUIDELINE FOR PREVENTION OF CATHETER-ASSOCIATED URINARY TRACT INFECTIONS 2009. Last update June 06 2019. https://www.cdc.gov/infectioncontrol/guidelines/cauti/
2. Jennifer Meddings; Sanjay Saint; Karen E. Fowler et al. The Ann Arbor Criteria for Appropriate Urinary Catheter Use in Hospitalized Medical Patients: Results Obtained by Using the RAND/UCLA Appropriateness Method. Ann Intern Med. 2015;162: S1-S34.
3. NHSG/ACCCG/GUI/001. Adult Catheterisation and Catheter Care Guidelines December 2017 Version 1. NHS Grampian.
4. Urinary Catheter Care Guidelines Version: 6 June 2020. NHS Southern health. NHS trust.

3.3.8 Venous thromboembolic disease (VTED) prevention

- See chapter VII. Hematologic disorders, topic 5 VTED, and sub topic 5.1 prevention of VTED

CHAPTER 4:

CARDIOVASCULAR DISORDERS

4.1. ARRHYTHMIAS

Brief description

- Arrhythmias are disorders of cardiac rate, rhythm and conduction.
- Bradyarrhythmias include sinus bradycardia, sinus pauses and atrioventricular blocks.
- The tachyarrhythmias can further be classified into supraventricular and ventricular arrhythmias, based on their site of origin.
- Supraventricular tachyarrhythmias includes atrial fibrillation, atrial flutter, paroxysmal supraventricular tachycardia and multifocal atrial tachycardia.
- Ventricular tachyarrhythmias include ventricular tachycardia and ventricular fibrillation.

THE ETIOLOGIES FOR ARRHYTHMIAS

- Structural heart disease (valvular heart disease, cardiomyopathies, coronary artery disease)
- Thyrotoxicosis
- Electrolyte abnormalities
- ingestion of stimulants
- Side effects of some medicines (digoxin, antiarrhythmic medicines

CLINICAL FEATURES OF ARRYTHMIAS IN GENERAL INCLUDE:

- Palpitation
- Shortness of breath

- Dizziness/syncope
- Sensation of a pause in the heart beat
- Chest discomfort that mimics symptoms of myocardial ischemia(angina)
- Development of Heart Failure or decompensation of previously existing Heart Failure
- Sudden death

DIAGNOSIS

- ECG is the main stay of diagnosis.
- Other investigations like Echocardiography, Chest X-ray, Thyroid function test, blood count, electrolytes should be guided by clinical data.
- Prior to treatment of any suspected arrhythmia the diagnosis should be confirmed with ECG.
    - It is dangerous to give any antiarrhythmic medicine without doing ECG!

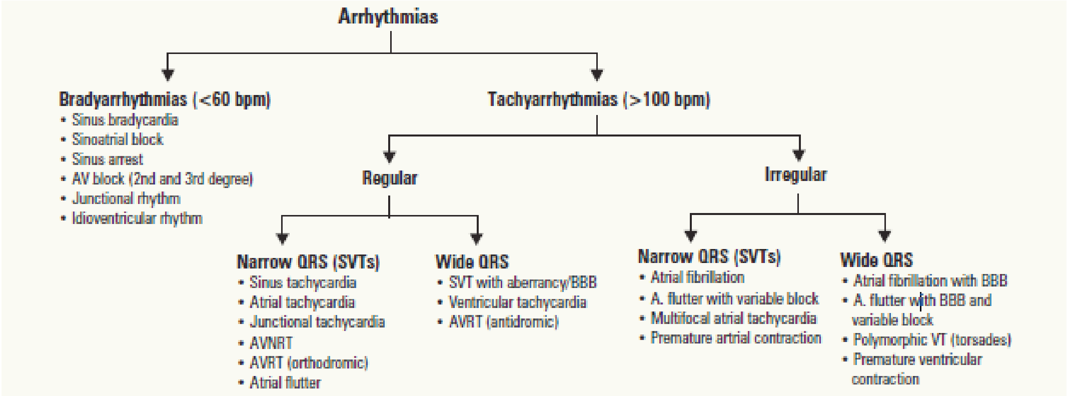

Arrhythmias
Bradyarrhythmias (<60 bpm)
• Sinus bradycardia
• Sinoatrial block
• Sinus arrest
• AV block (2nd and 3rd degree)
• Junctional rhythm
• Idioventricular rhythm
Tachyarrhythmias (>100 bpm)
Regular
Irregular
Narrow QRS (SVTs)
• Sinus tachycardia
• Atrial tachycardia
• Junctional tachycardia
• AVNRT
• AVRT (orthodromic)
• Atrial flutter
Wide QRS
• SVT with aberrancy/BBB
• Ventricular tachycardia
• AVRT (antidromic)
Narrow QRS (SVTs)
• Atrial fibrillation
• A. flutter with variable block
• Multifocal atrial tachycardia
• Premature artrial contraction
Wide QRS
• Atrial fibrillation with BBB
• A. flutter with BBB and variable block
• Polymorphic VT (torsades)
• Premature ventricular contraction

Figure 4.1: Clinical approach to arrhythmias (adopted from STG 3rd edition, 2014)

4.1.1. TACHYARRHYTHMIAS

SUPRAVENTRICULAR TACHYARRHYTHMIAS

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

BRIEF DESCRIPTION

- Paroxysmal supra-ventricular tachycardia (PSVT) is an intermittent narrow complex tachyarrhythmia other than AF, atrial flutter, and MAT (Multifocal Atrial Tachycardia).
- PSVT usually occurs in individuals without underlying structural heart disease.
- ECG shows regular narrow QRS tachycardia. P wave may be seen preceding or following or superimposed on QRS complex or may not be seen.

TREATMENT

Objectives of therapy include:

- Control ventricular rate
- Identify and treat the cause
- Identify, prevent and treat precipitating factors

NON-PHARMACOLOGIC

- Vagal maneuvers: maneuvers which increase vagal activity can terminate episodes of PSVT. ECG and blood pressure monitoring are required during the procedure.
    - Carotid sinus massage: supine position with the neck extended. The carotid sinus is located inferior to the angle of the jaw at the level of the thyroid cartilage. Steady pressure is applied to one carotid sinus for 5 to 10 seconds. If no response, repeat it in the contralateral side after 1-2 minutes.

Note: Carotid massage should not be attempted in patients with carotid bruit/ stenosis or ischemic stroke. Both carotid sinuses should never be massaged simultaneously.

  - Valsalva maneuver: while in the supine position the patient is instructed to exhale forcefully against a closed glottis with closed mouth and nose for 10 seconds. Adequacy indicated by neck vein distension, and increased tone in the abdominal wall muscles.

- Synchronized electrical Cardioversion: required rarely for hemodynamically unstable patients. The energy needed is 150 to 200 joules for monophasic defibrillators.

PHARMACOLOGIC TERMINATION OF ACUTE EPISODE

First line

- **Adenosine**, I.V, very rapidly (over 1-2 seconds): Initial: 6mg; if not effective within 1-2 minutes, 12mg may be given; may repeat 12mg bolus if needed. Follow each dose with 20mL very rapid Normal saline flush.

Alternatives

- **Metoprolol**, IV, 2.5-5mg every 2-5 minutes (maximum total dose: 15mg over a 10-15minute period).

OR

- **Verapamil**, I.V, 2.5-5mg over 2 minutes; second dose of 5-10mg may be given after 15-30 minutes; maximum total dose: 20-30mg

OR

- **Digoxin**, 0.5 to 1mg IV over a period of 10 to 15 min followed by 0.25mg every 2-4 hours with a total dose less than 1.5mg with in 24-hour period

PREVENTION OF RECURRENCE (CHRONIC THERAPY)

First line:

- **Metoprolol succinate** (Extended release): 25-200mg/day, P.O.

OR

- **Atenolol,** 25-100mg/day, P.O. or **Propranolol** 10-40mg P.O. 3-4 times daily

Alternatives

- **Verapamil,** immediate release 40-120mg, P.O.TID or extended release 180-360mg/day

ATRIAL FIBRILLATION AND FLUTTER

BRIEF DESCRIPTION

- Atrial fibrillation: is marked by disorganized, rapid, and irregular atrial activation which results in irregular ventricular response. The ventricular rate is usually rapid. The ECG in Atrial Fibrillation is characterized by the lack of P-waves, irregularly irregular ventricular response and narrow QRS.
- Atrial flutter: is characterized by regular rapid atrial rate of 260–300 beats per minute, which usually results in a regular ventricular response in a 2:1 ratio resulting in a heart rate of 130– 150 beats per minute. The ventricular response can sometimes be in 3:1, 4:1, irregular or rarely 1:1 ratio. The typical ECG finding is of saw-tooth appearance of the baseline mainly on inferior leads (II, III, AVF) with rapid, regular and narrow QRS.

TREATMENT

- The management of atrial fibrillation and atrial flutter are the same.

OBJECTIVES OF TREATMENT

- Controlling ventricular rate
- Prevention of thromboembolic events
- Identification and treatment of the cause
- Identification, prevention and treatment of precipitating factors

NON PHARMACOLOGIC

- Avoid stimulants (e.g., Caffeine, Khat) and alcohol intake.
- Immediate electrical cardio-version-associated with hemodynamic instability (cardiogenic shock) due to a rapid ventricular rate. If

hypotension occurs at ventricular rate <130 beats/min, other causes of hypotension should be investigated. The energy requirement is usually 100 to 200 joules; it should be synchronized.

PHARMACOLOGIC
ACUTE VENTRICULAR RATE CONTROL

First line:

- **Metoprolol,** 2.5-5mg, IV, over 3–5 min, to maximum total dose 15mg over 10-15 minutes

Alternative

- **Digoxin**, 0.25mg, IV, q2h until 1 mg total (digoxin is the first line medicine if atrial fibrillation is associated with severe left Ventricular dysfunction)

CHRONIC VENTRICULAR RATE CONTROL

First line:

- **Metoprolol,** preferred beta blocker in patients with Heart Failure with depressed LV (left ventricle) systolic function.
    - Immediate release: 25-100 mg twice daily
    - Extended release: 25-200mg/day

OR

- **Atenolol,** 25-100mg P.O., daily

Alternatives

- **Digoxin** 0.125 – 0.25mg P.O., daily. Digoxin can be added to beta blocker when the ventricular rate control is suboptimal. It is the preferred agent when Heart Failure due to LV systolic dysfunction is not well controlled.

OR

- **Verapamil,** 40-80mg P.O., 2-3 times daily.

ANTICOAGULATION TO PREVENT CARDIOEMBOLIC CEREBROVASCULAR ACCIDENT (CVA)

- Risk stratifies patients for thrombotic complications with the CHA2DS2-VASc score:
    - This is a scoring calculator used to estimate annual stroke risk in a patient with atrial fibrillation or atrial flutter.
    - It assigns 1 point each to presence of heart failure, HTN, age 65 to 74, diabetes, female sex, vascular disease, and 2 points each to age >75, and history of CVA.
    - The higher the score, the higher the annual stroke risk. For patients with CHA2DS2-VASc score >1, anticoagulation is generally indicated unless high bleeding risk.

Table 4.1: Scoring systems for assessing the risk of stroke (CHA2DS2-VASc) and bleeding (HAS-BLED) in patients with atrial fibrillation

CHA2DS2-VASc	Score	HAS-BLED	Score
Congestive heart failure	1	Hypertension (systolic blood pressure >160 mm Hg)	1
Hypertension	1	Abnormal renal and liver function (1 point each)	1 or 2
Age ≥75 years old	2	Stroke	1
Diabetes mellitus	1	Bleeding tendency/predisposition	1

Stroke/transient ischemic attack/ thromboembolism	2	Labile INRs (if on warfarin)	1
Vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque)	1	Elderly (e.g., age >65 years old)	1
Age 65–74 years old	1	Drugs or alcohol (1 point each)	1 or 2
Sex category (i.e., female sex)	1		
Maximum score	9	Maximum score	9

- Choice of anticoagulant: depends on etiology of AFib or atrial flutter.
    - For patients with mechanical valves, mitral valvular disease, or ventricular assist devices, warfarin is the only oral anticoagulant available. For other patients, direct oral anticoagulants (DOACs) can be used.
    - DOACs approved for AFib include factor Xa inhibitors (apixaban, rivaroxaban, edoxaban) and direct thrombin inhibitors (dabigatran). These agents do not require laboratory monitoring. Cost is the limiting factor for wider use in resource limited settings like Ethiopia.
    - Rivaroxaban is the available direct oral anticoagulant in Ethiopia.
    - The dose is Rivaroxaban 20 mg Po daily.
    - Dose adjustment is required for patients with renal failure, elderly, low body weight and those with high risk of bleeding.

- Warfarin: widely available and affordable anticoagulant. Warfarin has a narrow therapeutic range and during therapy monitoring using INR is mandatory. An INR of 2 to 3 is the anticoagulation goal range for warfarin. Warfarin, starting dose, 2.5-5mg/day, dose titrated to achieve INR of 2.0-3.0. The goal is to maintain time in therapeutic (TTR) range above 70 %.

Table 4.2: Warfarin dosing and monitoring

Suggested dose changes for maintaining INR within a target range of 2–3	
INR	Dose change
<1.5	Increase by 20%
1.6–1.9	Increase by 10%
3.1–3.4	Decrease by 10%, adjustment may not be necessary
3.5–3.9	Decrease by 20%, consider holding one dose
4.0–4.9	Hold dose until INR returns to range then decrease by 20–30%

Table 4.3: Management of supratherapeutic INR values

INR	Patient situation	Action
3.1–5.0	No bleeding or need for rapid reversal	Omit next few warfarin doses and/or re-start at lower dose when INR approaches desired range. If INR is only minimally above range, no dose reduction may be needed.
	(i.e., no need for surgery)	

5.1–9.0	No bleeding or need for rapid reversal	Omit next 1–2 doses, monitor INR more frequently, and restart at lower dose when INR approaches target range or omit dose and give 1-2.5 mg vitamin K orally (use this if patient has risk factor for bleeding).
	No bleeding but reversal needed for surgery or dental extraction within 24 hours	Vitamin K_1 2–4 mg orally (expected reversal within 24 hours); give additional 1–2 mg if INR remains high at 24 hours.
9.1–20.0	No bleeding	Stop warfarin; give vitamin K_1 3–5 mg orally; follow INR closely; repeat vitamin K_1 if needed. Reassess need and dose of warfarin when INR approaches desirable range.
Rapid reversal required (>20.0)	Serious bleeding or major warfarin overdose	Stop warfarin; give vitamin K_1 10 mg by slow IV infusion. May repeat vitamin K_1 every 12 hours and give fresh plasma transfusion or prothrombin complex concentrate as needed. When appropriate, heparin can be given until the patient becomes responsive to warfarin.
Life Threatening bleeding		Replace with prothrombin complex concentrate and give 10 mg of vitamin K_1 by infusion. May repeat if needed. Give fresh frozen plasma if prothrombin complex concentrates not available.

- In addition to stroke risk assessment, a discussion regarding anticoagulation should include an assessment of bleeding risk and involve shared decision making to take into account patient preferences.

- The HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs/alcohol concomitantly) score uses several common risk factors and provides an estimate of bleeding risk.

- The selection of an anticoagulant agent (warfarin or rivaroxaban) should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including time in the international normalized ratio (INR) therapeutic range (TTR) if the patient has been taking warfarin.

VENTRICULAR TACHYCARDIA

BRIEF DESCRIPTION

- Ventricular tachycardias are wide QRS tachyarrhythmias that originate in the myocardium.

- They are commonly associated with some form of structural heart disease.

- Based on their clinical significance, they can be divided in to two:

    - Malignant (potentially lethal) arrhythmias: sustained ventricular tachycardia (VT) and Ventricular fibrillation.

    - Non sustained (hemodynamically tolerated) arrhythmias: premature ventricular contractions (PVCs), non-sustained ventricular tachycardia (NSVT), and accelerated idioventricular rhythm (AIVR).

- A ventricular tachycardia which stays for more than 30 seconds is labeled sustained.

- All Wide QRS (> 120 ms) tachycardias are considered and treated as ventricular tachyarrhythmias until proved otherwise.

TREATMENT

Objectives of treatment

- Prevent degeneration of ventricular tachycardia to ventricular fibrillation.
- Reverse cardiac arrest

Non pharmacologic

- CPR should be provided to patients with sustained VT with cardiac arrest (the victim is unresponsive, pulseless and not breathing).
- O2 via face mask or nasal catheter.
- Continuous ECG monitor.
- Suction device and endotracheal intubation set should be ready.
- Correct electrolyte disorders.
- Reassure patients with non-sustained ventricular tachycardia.

Defibrillation:

- Sustained polymorphic VT, ventricular flutter, or ventricular fibrillation
- Emergency defibrillation (without synchronization), with >200 Joules (monophasic), increase the energy to the maximum if arrhythmia persists.
- Sustained monomorphic VT: synchronized with >200 Joules (monophasic).

Note:

  - If the hemodynamic status allows conscious sedation should be provided.

  - DC cardioversion is first line therapy for sustained wide QRS tachycardias.
  - Pharmacologic treatment may be an acceptable option in hemodynamically stable monomorphic VT with no Heart Failure.

PHARMACOLOGIC

FIRST LINE

INTRAVENOUS AMIODARONE

- Stable VT regimen:
  - *Step 1: 150mg over first* 10 minutes (dilute in 100mL D5W)
  - Step 2: 360mg over next 6 hours (dilute 500mL D5W): 1 mg/minute
  - Step 3: 540mg (dilute in 500 to 1000ml D5W) over next 18 hours: 0.5mg/minute
- Pulseless VT (cardiac arrest) regimen: If unresponsive to defibrillation attempts and CPR **Amiodarone**, I.V push, 300mg (undiluted), if VT or VF recurs, administer supplemental dose of 150mg and continue CPR.

Alternative

INTRAVENOUS LIDOCAINE

- Both stable VT and Pulseless VT (cardiac arrest) regimen:
  - **Lidoc**aine, I.V, 1-1.5mg/kg; repeat with 0.5-0.75mg/kg every 5-10 minutes if no response. (Maximum cumulative dose: 3mg/kg).
  - Follow with continuous infusion of 1-4mg/minute
  - Preparation for continuous infusion: 2g of lidocaine/250mL D5W

- o Rate of infusion: 1mg/min = 7.5ml/hour, 2mg/min =15ml/hour, 3mg/min= 22.5ml/hr, 4mg/min= 30ml/min

PREVENTION OF RECURRENCE

Non-pharmacologic

- Standard treatment of the underlying cause is the main stay of treatment for preventing recurrent VT. (e.g., treatment of acute coronary syndrome)
- Correct precipitating causes (e.g., hypoxia, hypo/hyperkalemia, acidosis, pulmonary embolism).
- Discontinue arrhythmogenic medicines-digoxin, antiarrhythmic medicines.

PHARMACOLOGIC

First line

- **Amiodarone,** P.O., 800-1600mg/day in 2 divided doses for 1-3 weeks, when adequate arrhythmia control is achieved, decrease to 600-800mg/day in 1-2 doses for 1 month. Maintenance: 400mg/day

Alternative or additional to Amiodarone

- Beta blockers: Metoprolol, extended release: P.O.,25-200mg/day or Atenolol, 25-100mg daily

Refer the patient to next care delivery after stabilization is strongly recommended.

4.1.2 BRADYCARDIA (BRADYARRHYTHMIA)

BRIEF DESCRIPTION

- AV block describes a delay/block of atrial impulses at the atrioventricular node of varying severity. When severe it results in symptomatic bradycardia which can manifest as easy fatigability, Heart Failure, syncope, seizures and bradycardia associated ventricular tachycardias.

- It is caused by structural heart diseases (mainly ischemic heart disease, cardiomyopathies, congenital heart disease), medicines (beta blockers, verapamil, digoxin), electrolyte abnormalities, hypothyroidism and cardiac surgery.
- ECG is the diagnostic of AV block.

TREATMENT

- Look for reversible causes and act accordingly
- Symptomatic bradycardia should be referred to the next health care facility for cardiologist evaluation.

4.2 HEART FAILURE

BRIEF DESCRIPTION

- Heart Failure is an abnormality of cardiac structure or function leading to failure of the cardiac output to meet the body's metabolic requirements despite normal filling pressures.
- Clinically it is a syndrome consisting of typical symptoms (shortness of breath, fatigue, orthopnea, ankle swelling) and signs (raised JVP, pulmonary crackles, displaced apex beat, edema).
- Identification of the underlying cause of the Heart Failure is central to diagnosis.
- It could result from valvular disease, ischemic heart disease, hypertension, cardiomyopathies, thyrotoxicosis, congenital heart disease, etc.

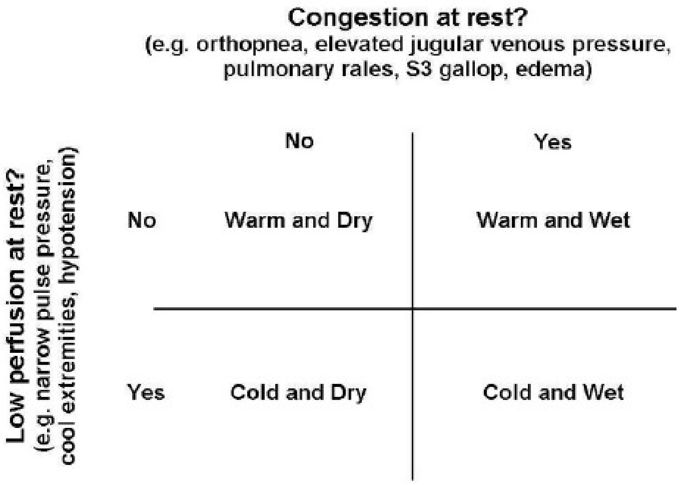
4.2.1 ACUTE HEART FAILURE

- **Definition**:The new onset or recurrence of gradually or rapidly developing symptoms and signs of HF requiring urgent or emergent therapy and resulting in hospitalization. It can be worsening of symptoms in known cardiac patients (the majority) or a new onset heart failure (Denovo).

- Acute heart failure syndromes are classified based on the relative absence and/or presence of congestion and hemodynamic compromise.

Key Questions

- Does the patient have heart failure?
- If so which syndrome among the acute heart failure syndromes?
- Is it a new onset or worsening of a previously known cardiac disease?
- Is there a treatable precipitating factor?
- Does the patient require admission to the ICU or a general medical ward?



Congestion at rest?
(e.g. orthopnea, elevated jugular venous pressure, pulmonary rales, S3 gallop, edema)

Low perfusion at rest? (e.g. narrow pulse pressure, cool extremities, hypotension)	No	Yes
No	Warm and Dry	Warm and Wet
Yes	Cold and Dry	Cold and Wet

Fig. 4.1: Hemodynamic classification of patients with acute heart failure

- Two-minute hemodynamic profile assessment: Patient presentation can be fitted in either of these syndromes.
- Warm=good systemic perfusion
- Cold=hypoperfusion (Cardiogenic shock CS=Cardiogenic shock
- Dry=No lung congestion
- Wet= Lung congestion (Pulmonary Edema (PE=Pulmonary Edema
- PE:Pulmonaryedema CS=Cardiogenic shock

- The following management approach works for all acute heart failure syndromes. Additional Specific management recommendations for pulmonary edema and cardiogenic shock are given separately.

CLINICAL FEATURES

- **Symptoms**: dyspnea, orthopnea, PND, cough, leg swelling, RUQ pain, abdominal distension
- **Signs**: tachycardia, tachypnea, high/normal/low BP, basal crepitations, pleural effusion, distended neck veins, raised JVP or Positive hepatojugular reflex, displaced AI, active/quite precordium, S3/S4 gallop, +/- murmurs, tender hepatomegaly, ascites, leg edema

- Factors leading to rapid deterioration
  - Tachy/brady arrhythmia
  - Acute Coronary Syndrome (ACS)
  - Acute pulmonary embolism
  - Hypertensive crisis
  - Cardiac tamponade
  - Aortic dissection

- Factors leading to less rapid deterioration
  - Non adherence to drugs/diet or under dosage
  - Infections (pneumonia, IE)
  - Anemia
  - Thyroid disorders
  - Pregnancy
  - Renal failure
  - Drugs (BB, CCB, NSAIDS)

○ Also look for precipitating factors through history and P/E

- Indications for admission to the ICU
  - Cardiogenic shock
  - Dyspnea at rest ($SO2 < 90\%$ which doesn’t improve with intranasal O2)
  - Hemodynamically significant arrhythmia
  - Acute Coronary Syndrome (ACS)
  - Hypertensive emergency
  - Altered mental status

- Indications for admission to General ward
  - Worsened congestion
  - Dyspnea at rest (tachypnea or $SO2< 90\%$) which improves with intranasal O2

INDICATIONS FOR ADMISSION

DIAGNOSIS

- **Diagnosis** of heart failure is clinical. But investigations are necessary to identify the underlying cause, precipitating factor, and to guide and monitor management.

• **To identify the underlying cause**: Echocardiography, ECG, CXR
• **To identify precipitating factors based on clinical evaluation** (in addition to the above investigations): CBC, ESR, U/A, blood culture, TFTs, Urine HCG, Cr, BUN, etc..
• **To guide and monitor management**: K+, Na+, Cr, BUN, ALT, AST

Class I	○ Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.
Class II	○ Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III	○ Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or angina.
Class IV	○ Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NEW YORK HEART ASSOCIATION (NYHA) CLASSIFICATION OF SEVERITY /FUNCTIONAL CAPACITY

Stage of Heart Failure

Stage A	High risk for HF, without structural heart disease or symptoms
Stage B	Heart disease with asymptomatic left ventricular dysfunction
Stage C	Prior or current symptoms of HF
Stage D	Advanced heart disease and severely symptomatic or refractory HF

TREATMENT

GOALS OF MANAGEMENT

- Improve symptoms (congestion and low output symptoms)
- Restore normal oxygenation
- Optimize volume status
- Identify and manage precipitating factor
- Identify etiology and manage if possible (e.g., ACS, arrhythmias)
- Optimize chronic oral therapy when needed
- **NB.** Management should be instituted **early** in parallel with the diagnostic work up. If patient has pulmonary edema or cardiogenic shock (*see the respective sections for initial management approach)*

Non-Pharmacologic

- Salt restriction (< 2gm or added salt), fluid restriction (< 1.5-2l/day) for hyponatremic patients
- Administer O_2 if SO_2< 90%.

Pharmacologic

- **Diuresis:**
    - Send sample for Cr, BUN, K+ and Na+ initially and proceed with diuresis.
    - For diuretic naive patients start furosemide 40 mg IV if BP>90/60 mmHg and double the dose every 2-4 hour until the urine output is >1 ml/kg/hr (40-70ml/hr). Response to IV dose occurs 2-4 hours later.
    - For those already on oral furosemide, start with equal dose of IV furosemide.
    - Maintain the dose of furosemide which gave adequate response on a TID basis.
    - Start spironolactone 25-50 mg/day unless K+> 5.0 meq/l or Cr> 1.6 mg/dl or GFR<30 ml/min (*main reason is to prevent hypokalemia due to furosemide*).
    - If patients were already talking ACEIs and BBs, they can continue to take them during hospitalization as long as they are not severely congested, are hemodynamically stable and have normal renal function.
    - Temporary discontinuation or dose reduction of BB may be necessary if BP is low or borderline and patient is severely congested (pulmonary edema).
    - Temporary discontinuation or dose reduction of ACEIs/ARBs may be necessary if BP is low or borderline and recent renal function derangement.
    - Manage the identified precipitating factors.

Follow up

- Use the standard heart failure management follow up sheet posted by the bedside.
- V/S including orthostatic hypotension and SO2 every 1hr until patient stabilizes and then every 4-6 hrs.
- 24 hrs urine output and fluid balance documented every 6hrs together with V/S.

- Weight every 24hrs (morning prior to eating and voiding, same scale).
  - Goal is 1kg/day weight loss
- Signs of heart failure every 12hrs (JVP, basal crackles, S3 gallop, hepatomegaly, edema).
- Symptoms **(dyspnea, orthopnea).**
- **Cr, BUN**, K+, Na+ every 24hrs until patient stabilizes and then every 3-5 days and manage accordingly

Table 4.4: Sample heart failure follow up form

Date	time	PR	RR	BP	T	Wt	SO2	UOP	Creps	Hepato megaly	JVP	Edema	Cr	Na+	K+	sign

Goal of diuresis

- Negative fluid balance
- Weight loss (0.5-1kg/day)
- Clearance of crepitations in the lungs
- Decrement in edema, hepatomegaly, JVP
- Improvement of dyspnea, orthopnea Improvement in renal function (Cr, BUN)

Signs of excess diuresis

- Signs of dehydration
- Hypotension(overt/orthostatic)
- Elevated RFTs despite improvement of congestion
- Severe hypokalemia

Patient not responding

- Make sure that
  - Patient is taking medications as prescribed and is on salt free diet.
  - Precipitating factors is managed.
  - Patient is not getting drugs like NSAIDS, CCBs, BBs.
    - NB: *Patients with deranged renal function and hypoalbuminemia require higher doses of frusemide from the outset.*
- Adjust the diuresis
  - Increase the dose of furosemide (max. 400-600mg/day) and increase spironolactone to 50-100mg/day.
  - Increase the frequency of administration of furosemide 4-6 times per day. Repeated IV bolus doses are recommended that continuous infusion.
  - In ICU continuous furosemide infusion by perfuser according to protocol: (10-80mg/hr) can be used if still refractory to the above measures.
  - If patient not responding with the above approaches, add hydrochlorthiazide 12.5 mg/day in the morning 30 minutes before frusemide administration.
- **Digoxin** 0.125-0.25 mg/day for positive inotropy and rate control in patients with atrial fibrillation.
  - For patients with hypertension and severe Acute MR intravenous nitroglycerin infusion can be considered in addition to diuretics. *(See pulmonary edema section)*

PATIENT IMPROVING

- Decrease the dose of diuretics every day depending on patient condition.
  - The goal is to use the lowest possible dose and frequency to keep patient dry.

- For patients in whom previous BB and ACEIs/ARBs have been discontinued consider reinitiating the drugs as soon as possible sequentially (ACEIs/ARBs followed by B blockers)
- For HFrEF previously not taking ACEIs/ARBs or BB.
    - Start one of the ACEIs/ARBs as soon as BP and RFTs permit and escalate until discharge (see chronic heart failure section)
    - Start one of the BB following ACEIs/ARBs when BP and PR permit and escalate until discharge (see chronic heart failure section)
    - Start Spironolactone 25mg/d.
- Change IV furosemide to PO and observe the patient with ambulation for a day or two.

Patients requiring higher dose of furosemide may require a double dose.

- Institute further management for the underlying heart disease *(see specific topic and comorbidities*

Before Discharge

- *Proper advice: salt consumption, activity, adherence to medications and follow up.*
- *Prescribe adequate medications and give requests for further planned outpatient investigations.*
- *Document medications with dose and further plans clearly on the discharge note.*
- *Early appointment preferably in one week time to follow up clinic.*

4.2.2 PULMONARY EDEMA

BRIEF DESCRIPTION

- Principles of management and follow up is similar but more frequent than other AHF syndromes.

- Early oxygenation and ventilation support is lifesaving.
- Treatable precipitating causes (e.g., Arrhythmia, hypertensive crisis, ACS) should be looked for and managed promptly

CLINICAL FEATURES

- Rapid development of dyspnea at rest
- cardiorespiratory distress
- Tachypnea
- SO2< 90%
- High/normal BP
- crepitations and wheeze in the lung
- Raised JVP, S3 gallop
- Treatable causes of pulmonary edema (eg. Hypertensive emergency, ACS, arrhythmia like AF) should be seriously looked for and managed according to the respective protocol together with management of pulmonary edema.

TREATMENT

Non pharmacologic

- **Oxygenation**
  - Sitting position
  - If SO2< 90%, administer O2 by nasal canula at 4-6 l/min.
  - If SO2 doesn't improve in 10 min, administer high flow O2(10-12 l/min) by face mask.
  - If SO2 is still low, give ventilator support by CPAP in conscious cooperative patients or intubate if patient cannot protect his /her airways and put on MV with low PEEP.
  - If SO2 is persistently higher than 90% and cardiorespiratory distress improves with treatment, revert O_2 administration to nasal canula and

progressively decrease O_2 flow and discontinue

PHARMACOLOGIC

- Administer **morphine** 2-4 mg IV bolus every 2-4 hr.
- **Furosemide** 40mg IV for naïve (intravenous dose which is equal to their previous oral dose for those already taking oral furosemide) and double the dose every 1hr until adequate urine output AND crackles in the chest start to decrease and maintain the dose of furosemide that gave adequate response every 4hrs for the first 24 hr and decrease frequency in subsequent days.
- Follow up of response and other management principles are similar to management of other acute heart failure syndromes (*see acute heart failure section*)
- For patients not responding adequately to diuretics with systolic BP >110mmHg, the following vasodilator therapies can be used:
    - Intravenous nitroglycerine infusion started with 10-20ug/min and escalated to 200ug/min depending on response and development of hypotension can be used.
    - If nitroglycerine not available, either of the following can be tried;
        - **Isosorbide dinitrite** 10mg po TID (8AM, 1PM and 6PM) escalated to 40mg po TID *or*
        - **Captopril** 12.5 mg or enalapril 2.5 mg and increase dose every 6hrs depending on response.

4.2.3 CARDIOGENIC SHOCK

BRIEF DESCRIPTION

- Systemic hypoperfusion secondary to decreased cardiac output and sustained systolic BP less than 90 mmHg despite an elevated filling pressure with evidence of organ hypoperfusion.

CLINICAL FEATURES

- Apprehensive and diaphoretic,
- Cold extremity,
- Poor capillary refill,
- Change in mentation,
- Systolic BP< 90mmhg,
- Decreased Urine output,
- Symptoms and signs of heart failure
- Inquire for history of fluid loss (vomiting, diarrhea, bleeding)

TREATMENT

Non pharmacologic

- Administer O_2 if SO_2<90%

PHARMACOLOGIC

- Administer **NS** 250ml over 30 min and see the change in BP, UOP and worsening of HF.
  - If BP improves then consider hypovolemic shock and continue slowly replacing the fluid with NS.
  - No response to fluid or worsening heart failure, use either of the following vasopressor therapies:
    - **Norepinephrine** 0.2 ug/kg/min escalated to 1ug/kg/min by doubling the dose q20 min until BP> 90/60 mmHg. Maintain the dose that maintained the BP> 90/60 mmHg
    - Alternative
    - **Dopamine** infusion at 5ug/kg/min and escalate to 40ug/kg/min by doubling the dose q20 min until BP> 90/60 mmHg. Maintain the dose that maintained the BP> 90/60 mmHg.

- If patient has concomitant pulmonary edema resulting in hypoxia
    - Continuous infusion of frusemide started at 5-10 mg/hr should be started through another IV line (escalate dose based on Blood Pressure).
    - Taper the dose of vasopressor in the same way as it was escalated if BP is maintained.
- More frequent follow up of V/S, SO2 and UOP q 20-30min until patient stabilizes
- Further follow up and management is similar to other heart failure syndromes.

4.2.4 CHRONIC HEART FAILURE

BRIEF DESCRIPTION

- This guideline focuses on the management and follow up of non-rheumatic chronic heart failure in those with depressed LV function (EF<40%). Management of chronic rheumatic valvular heart disease is given separately.

AT FIRST ENCOUNTER:

History:

- Low output: fatigue, weakness, exercise intolerance, change in mental status, anorexia
- Congestive: left sided: dyspnea, orthopnea, PND
- Right sided: peripheral edema, RUQ discomfort, bloating, satiety
- Functional classification: using NYHA classification
- Stage the disease: see below

DIAGNOSTIC WORK UP:

- Basic: CXR, ECG, Echocardiography
- Lab tests: BUN, Cr, electrolyte, urinalysis, FBS, lipid profile

- Evaluate for possible risk factor and treat.
- Follow steps in the management of Heart Failure with Reduced Left Ventricular Systolic Function

OBJECTIVES:

Relieve symptoms, reduce hospitalization, improve survival, reduce complications

- Step 1: Start low dose ACEs
- Step 2: review after two weeks: Check tolerance and side effects
    - BP, symptoms
    - Side effects ACEs
- Step 3: Increase dose of ACEs
    - If there is troubling cough related to the ACEs (not because of heart failure), switch therapy to ARBs
- Step 4: review after one month and assess for Beta blocker therapy
    - If a candidate; start low dose Betablocker
- Step 5: Review after two weeks for assessment
    - If tolerated, increase dose
- Step 6: Review heart failure status (symptom, NYHA class, congestion)
    - Optimize therapy as per evidences
- Step 7: Monitor therapy at each visit (RFT, Electrolytes, optimize risk factors)
- Step 8: Early referral for refractory cases for cardiologist evaluation

Table 4.5: Management of heart failure	
• Diet, exercise	• Avoid table salt intake, alcohol and smoking • Avoid stimulant caffeine other like khat, marijuana Avoid excess free water consumption • Exercise training in ambulating patients
• ACEI • Optimal doses are more efficacious • Watch for azotemia, increased K+, cough, angioedema • Contraindicated; pregnancy, renal artery stenosis, hyperkalemia	• Escalate every 1-2 week • Enalapril dose 2.5mg/day - 20mg BID • Alternative • Lisinopril dose 10-40mg/day
• ARBs (ATII receptor blockers) • Alternative to ACEI (cough, angioedema) but not a substitute • Others same with ACEI	• Candesartan 8-32 mg/day in 1-2 divided doses • Alternative • Valsartan 40 -80 mg PO BID
ARNI (Angiotensin-Neprolysin Inhibitors	• Sacubutril/Valsarthan combination starting with 50 mg (24/26) PO BID to increase to the most tolerable dose of 200 mg (97/103) PO BID
• Beta- blockers • High doses are more efficacious • Caution: severe COPD/asthma, AV block(bradycardia), hypotension(shock)	• Preferred: (long releasing and escalate every 2 week) • Metoprolol dose 6.75 - 200mg per day • Carvedilol dose 3.125-25mg BID • Bisoprolol 1.25 mg Po-10 mg Po daily • Nebivolol 1.25 mg PO-10 mg Po daily

• Aldosterone antagonist • Consider in severe HF or post MI • Caution: renal function, Increased K	• Spironolactone 25mg po per day • NB: 50mg/day patients with high dose furosemide and hypokalemia
• Diuretics • Patients with congestion (ie. Not only right sided but also orthopnea, PND, nocturnal cough) • Watch electrolyte (Na, K, Cl) and BUN, Cr	• Loop diuretics • Lasix(furosemide) 20mg/day up to 100-120mg TID/QID (preferred to keep low dose) • Thiazide:HCT 12.5-25mg per day (congestion not improved with high dose lasix) see diuretic resistance
• Digoxin • Caution: renal failure, hypokalemia, Rheumatic heart disease (MS) • Use: rate control in AFFVR and added on therapy	• Dose 0.125-0.25mg per day

In every follow up visit:

Assess	Manage
• Symptoms • Functional status • Adherence • Medication tolerance • P/E: V/S, signs of heart failure, precordial exam • Investigations: Cr, BUN, K+, Na+ as appropriate	• Escalate dose of ACEIs and BBs if no problem • Consider add on therapies like spironolactone, digoxin if patient not improving after optimal diuretic, ACEI and BB therapy • on adherence to treatment and life style modifications

FURTHER READING

1. ACC/AHA Guideline for the management of Heart Failure, 2016
2. ESC Guideline for the management of Heart Failure, 2016

4.3 HYPERTENSION

BRIEF DESCRIPTION

- Hypertension is a serious medical condition that significantly increases the risks of heart, brain, kidney and other diseases. According to the WHO STEPS survey the prevalence of hypertension in Ethiopia is 16%.
- In Ethiopia and other low- and middle-income countries, there is a wide gap between evidence- based recommendations and current practice. Treatment of major CVD risk factors remains suboptimal, and only a minority of patients who are treated reach their target levels for blood pressure, blood sugar and blood cholesterol.

HYPERTENSION DETECTION AND TREATMENT

When to measure blood pressure

- Measuring blood pressure is the only way to diagnose hypertension, as most people with raised blood pressure have no symptoms.
- Blood pressure measurements should be conducted on all patients during health facility visits as part of the vital sign. Every patient with elevated blood pressure readings requires immediate follow-up, according to the protocol. More frequent blood pressure measurements and control is particularly important in adults who:
    - Have had a prior heart attack or stroke
    - Have diabetes
    - Have chronic kidney disease (CKD)
    - Are obese
    - Use tobacco
    - Have a family history of heart attack or stroke

HOW TO MEASURE BLOOD PRESSURE

- Effective treatment algorithms for hypertension are dependent on accurate blood pressure measurement. The following advice should be followed for measuring blood pressure:
  - Use the appropriate cuff size, noting the lines on the cuff to ensure that it is positioned correctly on the arm. (If the arm circumference is >32 cm, use large cuff.)
  - On initial evaluation it is preferable to measure blood pressure on both arms and use the arm with the higher reading thereafter
  - The patient should be sitting with back supported, legs uncrossed, empty bladder, relaxed for 5 minutes and not talking.
  - It is preferable to take at least two readings at each occasion of measurement and to use the second reading.
  - Blood pressure can be measured either by a conventional sphygmomanometer, using a stethoscope, or by an automated electronic device. The WHO recommended calibrated electronic device, if available, is preferred because it provides more reproducible results and is not influenced by variations in technique or by the bias of the observers.

DIAGNOSING HYPERTENSION

- The diagnosis of hypertension should be confirmed at an additional patient visit, usually 1 to 4 weeks after the first measurement depending on the measured values and other circumstances. In general, hypertension is diagnosed if, on two visits, on different days:

Clinical Condition	Office Blood Pressure Measurement			
	< 140/90	140-159/90-99	160-179/100-109	≥180/110
If there is no evidence of end-organ damages	Re-measure after 1year	Confirm in one Month	Confirm as soon as possible within one week	Diagnose HTN and refer to specialist
If there is evidence of end-organ damages	Confirm HTN and refer to specialist			
Hypertensive Crises (BP> 180/110 mmHg) with or without target organ damage				

- ○ Systolic blood pressure on both days is ≥140 mmHg and/or diastolic blood pressure on both days is ≥90 mmHg.
- ○ Once diagnosis of hypertension is made:

- **Look for end-organ damage based on:**
  - ○ **History**: Symptoms of heart failure (SOB, unusual fatigue and body swelling), history of sudden onset body weakness (stroke), intermittent claudication or previous diagnosis of the above problems on previous evaluation at other health institutions, severe headache and blurring of vision.
  - ○ **Physical Examination**: Pulse rate and rhythm, signs of heart failure (edema, elevated JVP, crackles on the lungs), Focal neurologic deficit, eye signs. The physical examination should be done to the maximum capacity of the health work force including fundoscopic retinal examination if possible.
  - ○ **Laboratory and other diagnostic tests**: Health facilities should thrive to avail at east mandatory tests. Please note that waiting for

laboratory tests shouldn't delay the intervention of hypertension as the disease do much harm than the extra benefit obtained from the tests. The tests are categorized as follows:

- **Mandatory tests at diagnosis**: urine dipstick to check for protein, Creatinine to check for renal function
- **Optional tests at diagnosis**: ECG to look for effect of blood pressure on the heart, Serum electrolytes mainly potassium, Thyroid function test to assess a secondary cause of hypertension
- **Indication based tests**: Echocardiography for heart failure patients, brain imaging for suspicion of stroke
- **Comorbidity and risk factor assessment tests:** Blood sugar and cholesterol

- **Look for risk factors:**
  - **History**: Smoking, excess salt intake, sedentary life, low fruit and vegetable intake, excess alcohol consumption
  - Physical **Measurement**: Weight, height, abdominal circumference,
- Calculate BMI: weight in kg / square root of height in meter
- **Cardiovascular Risk assessment**; For all patients found to have raised BP, their future 10-year cardiovascular risk should be assessed by using WHO CV risk score (Refer WHO CV risk assessment manual). In a setting where serum cholesterol and fasting blood glucose can be determined use the laboratory-based risk assessment. If laboratory assessment service is not available, the non-laboratory-based risk chart.

Hypertension Treatment

Who should receive hypertension treatment?

- Hypertension treatment is indicated for adults diagnosed with hypertension, as defined above (SBP ≥140 mmHg and/or DBP ≥90 mmHg). Patients with SBP ≥180 mmHg or DBP ≥110 mmHg may be indicated for immediate treatment based on one assessment.

- Lifestyle counseling (healthy diet, physical activity, tobacco use, and harmful use of alcohol) is a critical component of good hypertension management and is often recommended as a first step for patients with blood pressure of SBP 130–139 mmHg and/or DBP 80–89 mmHg who do not have other CVD risk factors. However, in settings where people do not regularly visit the doctor, people who are recommended only lifestyle modification may not return for re-evaluation and needed treatment, resulting in uncontrolled hypertension and associated complications.

NON PHARMACOLOGIC (LIFE STYLE INTERVENTIONS)

- All patients diagnosed to have hypertension should be given lifestyle interventions which include:
  - Consume healthy diet
  - Engage in physical activity
  - Avoid smoking
  - Limit use of alcohol
- Pharmacologic (Drug Treatment): Indications;
  - Patient who couldn't achieve target blood pressure with life style interventions.
  - At initial presentation in those with:
  - End-organ damage or high WHO cardiovascular risk (>20%)
    - Hypertensive Crises (see below)

TREATMENT TARGETS

- For most patients, blood pressure is considered controlled when SBP <140 mmHg and DBP <90 mmHg.

Life style intervention

- Life style intervention should be implemented in all grades of hypertension. For uncomplicated grade I hypertension life style intervention can be tried for three months before initiation of medications. If failed to achieve a blood pressure of less than 140/90 mmHg, then initiation of antihypertensive medication is recommended.

WHAT MEDICATIONS SHOULD BE USED TO TREAT HYPERTENSION?

INITIAL MONOTHERAPY IN UNCOMPLICATED HYPERTENSION:

- Long-acting dihydropyridine **calcium channel blocker** such as amlodipine as first line drug for the treatment of uncomplicated essential hypertension in our country at General Hospital level as it is the most extensively studied drug with evidence. It is probably effective for all races; reduces need for monitoring of electrolytes and renal function; avoids need for different treatment for women of childbearing age who may become pregnant.
    - Dose: **Amlodipine** 5 mg daily, escalate to 10 mg if BP is uncontrolled.
- Thiazide diuretics such as hydrochlorothiazide to be used as add on when target BP not achieved on long-acting dihydropyridine calcium channel blocker such as amlodipine it is less expensive than other hypertension medications in our setting and are probably effective for all races. Because of the lack of evidence with the readily available thiazide diuretics such as hydrochlorothiazide as monotherapy with regards to CVD event reduction, the risk of hypokalemia and the unfavorable effects on lipid and glucose associated with the drug which necessitates laboratory monitoring, we suggest to be used as add on.
    - Dose: **Hydrochlorothiazide** *25 mg Po daily*
- If a third agent is needed, the alternative class of medication is ACE inhibitors considering cost of the drug and availability at the General Hospitals in Ethiopia. Lisinopril is the preferred drug in this class due to its ease of administration. The alternative is Enalapril.
    - ***Dose:* Lisinopril** 5 mg daily, escalate dose to 40 mg Po daily if BP is uncontrolled
    - ***Enalapril*** *5 mg Po BID, escalate to 20 mg Po BID if BP is uncontrolled*

NOTES ON SPECIFIC HYPERTENSION MEDICATIONS

- Pregnant women and women of childbearing age not on effective contraception should *not* be given ACE inhibitors, ARBs, or thiazide/ thiazide-like diuretics; CCBs should be used. If not controlled with intensification dose of medication, refer to specialist. Please refer to the Hypertension and Pregnancy module for the management of such cases.
- Beta blockers are not recommended as first-line therapy. If a heart attack has been diagnosed within the previous three years, or there is atrial fibrillation or heart failure, then a beta blocker should be added to the starting dose of antihypertensive medication. Patients with angina may also benefit from treatment with a beta blocker.

TREATMENT ADHERENCE

- Adherence to treatment is critical for blood pressure control. If antihypertensive medication is being prescribed, the following are critical to ensuring adherence:
  - Teach the patient how to take the medications at home.
  - Explain the difference between medicines for long-term control (for example, of blood pressure) and medicines for quick relief (such as for headaches).
  - Explain the reason for prescribing the medicine(s).
  - Explain the diagnosis of hypertension.
  - Discuss the asymptomatic nature of hypertension and explain that medications must be taken even if there are no symptoms.
    - Inform patient of the complications of untreated hypertension, including stroke, heart attack, and kidney failure.
    - Explain the disability and economic and family burden these preventable complications cause.
    - Show the patient the appropriate dose.
    - Explain how many times a day the patient should take the medication and at what time, and adopt the following simple

steps to help them to adhere to the guidelines:

  - Label and package the tablets.
  - Check the patient's understanding before the patient leaves the hospital.
  - Wherever possible, use once-daily dosages of all medications, to be given at the same time each day.

- Explain how important it is for the patient to:
  - Keep an adequate supply of medications safely at home.
  - Take the medicines regularly as advised, even if there are no symptoms.
  - Explain potential adverse effects of the medications and what to do if the patient experiences them.

4.3.1 COMMON COMORBIDITIES AND COMPLICATIONS

BRIEF DESCRIPTION

- Hypertensive patients have several common and other comorbidities that can affect cardiovascular risk and treatment strategies.
- The number of comorbidities increases with age, with the prevalence of hypertension and other diseases.
- Common comorbidities include coronary artery disease (CAD), stroke, CKD, HF, and COPD.
- Uncommon comorbidities include rheumatic diseases and psychiatric diseases.
- Common and uncommon comorbidities should be identified and managed according to available evidence.
- **Hypertension and Coronary Artery Disease (CAD)**
  - A strong epidemiological interaction exists between CAD and hypertension that accounts for 25%–30% of acute myocardial infarctions.

  - Lifestyle changes are recommended (smoking cessation, diet and exercise).
  - BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
  - *Refer coronary artery disease protocol*
- **Hypertension and Previous Stroke**
  - Hypertension is the most important risk factor for ischemic or hemorrhagic stroke
  - Stroke can be largely prevented by BP control.
  - BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
  - *Refer stroke protocol*
- **Hypertension and Heart Failure (HF)**
  - Hypertension is a risk factor for the development of HF with reduced ejection fraction (HFrEF), and with preserved ejection fraction (HFpEF). Clinical outcome is worse and mortality is increased in hypertensive patients with HF.
  - Lifestyle changes are recommended (diet and exercise).
  - Treating hypertension has a major impact on reducing the risk of incident HF and HF hospitalization. BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg but >120/70 mm Hg.
  - Refer *to the Heart failure protocol*
- **Hypertension and Chronic Kidney Disease (CKD)**
  - Hypertension is a major risk factor for the development and progression of albuminuria and any form of CKD.
  - A lower eGFR is associated with resistant hypertension, masked hypertension, and elevated nighttime BP values.
  - The effects of BP lowering on renal function (and albuminuria) are

dissociated from cardiovascular benefit.

  - BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
  - Refer the *CKD protocol*

- **Hypertension and Chronic Obstructive Pulmonary Disease (COPD)**
  - Hypertension is the most frequent comorbidity in patients with COPD.
  - BP should be lowered if ≥140/90 mm Hg and treat- ed to a target <130/80 mm Hg (<140/80 in elderly patients).
  - Lifestyle changes (smoking cessation) are mandatory.
  - Environmental (air) pollution should be considered and avoided if possible.
  - Refer the *COPD Protocol*
- **Diabetes**
  - BP should be lowered if ≥140/90 mm Hg and treat- ed to a target <130/80 mm Hg (<140/80 in elderly patients).
  - The treatment should include glucose and lipid lowering as per current guidelines.
  - Refer Diabetes *protocol*
- **Metabolic Syndrome (MS)**
  - Patients with hypertension and MS have a high-risk profile.
  - The diagnosis of MS should be made by separate evaluation of single components.
  - The treatment of MS is based on changes in lifestyle (diet and exercise).
  - The treatment of hypertension and MS should include BP control as in the general population and treatment of additional risk factors based on level and overall cardio- vascular risk.

- *Refer WHO cardiovascular risk prediction chart and accompanied protocol*

4.3.2 HYPERTENSIVE EMERGENCIES

DEFINITION OF HYPERTENSIVE EMERGENCIES AND THEIR CLINICAL PRESENTATION

- A hypertensive emergency is the association of substantially elevated BP with acute Hypertension Mediated Organ Damage (acute HMOD). Target organs include the retina, brain, heart, large arteries, and the kidneys.
- This situation requires rapid diagnostic workup and immediate BP reduction to avoid progressive organ failure. Intravenous therapy is usually required. The choice of antihypertensive treatment is predominantly determined by the type of organ damage. Specific clinical presentations of hypertensive emergencies include:
    - **Malignant hypertension:** Severe BP elevation (commonly >200/120 mm Hg) associated with advanced bilateral retinopathy (hemorrhages, cotton wool spots, papilledema).
    - **Hypertensive encephalopathy:** Severe BP elevation associated with lethargy, seizures, cortical blindness and coma in the absence of other explanations.
    - **Hypertensive thrombotic microangiopathy:** Severe BP elevation associated with hemolysis and thrombocytopenia in the absence of other causes and improvement with BP-lowering therapy.
    - Other presentations of hypertensive emergencies include severe BP elevation associated with cerebral hemorrhage, acute stroke, acute coronary syndrome, cardio- genic pulmonary edema, aortic aneurysm/ dissection, and severe preeclampsia and eclampsia.
    - Patients with substantially elevated BP who lack acute HMOD are not considered a hypertensive emergency and can typically be treated with oral antihypertensive therapy

CLINICAL PRESENTATION AND DIAGNOSTIC WORKUP

- The clinical presentation of a hypertensive emergency can vary and is mainly determined by the organ(s) acutely affected. There is no specific BP threshold to define a hypertensive emergency.
- Symptoms include headaches, visual disturbances, chest pain, dyspnea, neurologic symptoms, dizziness, and more unspecific presentations.
- Medical history: preexisting hypertension, onset and duration of symptoms, potential causes (nonadherence with prescribed antihypertensive drugs, lifestyle changes, concomitant use of BP elevating drugs [NSAIDS, steroids, immunosuppressants, sympathomimetics, cocaine, antiangiogenic therapy]).

DIAGNOSTIC TESTS AND ACUTE THERAPEUTIC MANAGEMENT

- The overall therapeutic goal in patients presenting with hypertensive emergencies is a controlled BP reduction to safer levels to prevent or limit further hypertensive damage while avoiding hypotension and related complications.
- There is a lack of randomized controlled trial data to provide clear cut guidance on BP targets and times within which these should be achieved. Most recommendations are based on expert consensus. The type of acute HMOD is the main determinant of the preferred treatment choice.
- The timeline and magnitude of BP reduction is strongly dependent on the clinical context. For example, acute pulmonary edema and aortic dissection require rapid BP reduction, whereas BP levels not exceeding 220/120 mm Hg are generally tolerated in acute ischemic stroke for certain periods. The table below provides a general overview of timelines and BP targets as well as preferred antihypertensive drug choices with most common clinical presentations.
- Availability of drugs and local experience with individual drugs are likely to influence the choice of drugs.
- *See Table below for locally adopted agents for BP lowering during Hypertensive Emergency*

FOLLOW-UP

- Patients who experienced a hypertensive emergency are at increased risk of cardiovascular and renal disease.
- Thorough investigation of potential underlying causes and assessment of HMOD is mandatory to avoid recurrent presentations with hypertensive emergencies.
- Regular and frequent follow-up (monthly) is recommended until target BP and ideally regression of HMOD has been achieved.

Table 4.6: Hypertensive Emergencies Requiring Immediate BP Lowering

Clinical Presentation	Timeline and Target BP	First Line Treatment	Alternative
• Malignant hypertension with or without thrombotic microangiopathy or acute renal failure	• Several hours, MAP −20% to −25%	• Labetalol	• Hydralazine
• Hypertensive encephalopathy	• Immediate, MAP −20% to −25%	• Labetalol	• Hydralazine
• Acute ischemic stroke and SBP >220 mm Hg or DBP >120 mm Hg	• 1 h, MAP −15%	• Labetalol	• Hydralazine
• Acute ischemic stroke with indication for thrombolytic therapy and SBP >185 mm Hg or DBP >110 mm Hg	• 1 h, MAP −15%	• Labetalol	• Hydralazine

• Acute hemorrhagic stroke and SBP >180 mm Hg	• Immediate, 130<SBP<180 mm Hg	• Labetalol	• Hydralazine
• Acute coronary event	• Immediate, SBP <140 mm Hg	• Nitroglycerine	
• Acute cardiogenic pulmonary edema	• Immediate, SBP <140 mm Hg	• Nitroglycerine (with loop diuretic)	• Loop diuretic
• Acute aortic disease	• Immediate, SBP <120 mm Hg and heart rate <60 bpm	• Nitroglycerine and metoprolol	• Labetalol or metoprolol
• Eclampsia and severe preeclampsia/ HELLP	• Immediate, SBP <160 mm Hg and DBP <105 mm Hg	• Labetalol and magnesium sulphate	• Hydralazine or short acting nifedipine

4.4 ATHEROSCLEROTIC CARDIOVASCULAR DISEASES

ISCHEMIC HEART DISEASE

Chest Pain (Approach and work up)

- Chest pain is one of the cardinal symptoms of cardiovascular disease, but it may also be present in many non-cardiovascular diseases.

Differential Diagnosis

- Heart, pericardium, vascular causes:
  - Stable angina, variant angina
  - Acute Coronary Syndrome (ACS)

  - Pericarditis
  - Aortic dissection
- Pulmonary:
  - Pulmonary embolism
  - Pneumothorax
  - Pleuritis (pleural pain)
  - Pneumonia
  - Status asthmaticus
- Gastrointestinal:
  - Gastroesophageal reflux disease (GERD)
  - Diffuse esophageal spasm, Peptic ulcer disease
  - Esophageal rupture
- Chest wall:
  - Costochondritis
  - Muscle strain
  - Rib fracture
  - Herpes zoster
- Psychiatric:
  - Panic attacks
  - Anxiety
  - Somatization

Approach to Treating a Patient with Chest Pain

- Rule out any life-threatening causes. These include ACS, aortic dissection, pericarditis with cardiac tamponade, pulmonary embolus, tension pneumothorax, and esophageal rupture

- Assess vital signs
- Develop a focused history
    - Character of the pain (pressure, squeezing, tearing, sharp, stabbing, etc.)
    - Location of pain
    - Severity of pain
    - Duration of pain
    - Setting in which pain occurred (during exertion, at rest, after meal)
    - Radiation of pain
    - Aggravating or alleviating factors (e.g., meal, exertion, rest, respiration)
    - Does the patient have a cardiac history? Ask about results of previous stress tests, echocardiograms, cardiac catheterization, or of any procedures (PCI or CABG)
    - If the patient has a *history of angina, ask how this episode differs from previous ones (more severe? longer duration?)*
- Perform a focused physical examination, with attention to cardiopulmonary, abdominal, and musculoskeletal examination
- Investigation: focused
    - Obtain ECG in almost all cases
    - Cardiac enzymes (CK, CK-MB, troponin) depending on clinical suspicion
    - Obtain chest radiograph (CXR) in a supportive clinical data
    - Under appropriate clinical setting, work up the patient for pulmonary embolism (PE) *(see Pulmonary section)*

4.4.1 CHRONIC CORONARY SYNDROME

- Chronic Coronary Syndrome is due to usually due to atherosclerotic lesions that narrow the major coronary arteries. Coronary ischemia is due to an imbalance between blood supply and oxygen demand, leading to inadequate perfusion. Stable angina occurs when oxygen demand exceeds available blood supply.

- **Major risk factors**
    - Diabetes mellitus (DM)—worst risk factor
    - Hyperlipidemia—elevated low-density lipoprotein (LDL)
    - Hypertension (HTN)—most common risk factor
    - Cigarette smoking
    - Age (men >45 years; women >55 years)
    - Family history of premature coronary artery disease (CAD) or myocardial infarction (MI) in first-degree relative: Men <55 years; women <65 years
    - Low levels of high-density lipoprotein (HDL)
    - Less common risk factors include:
        - End-stage renal disease (ESRD) on hemodialysis,
        - Human immunodeficiency virus (HIV) infection,
        - History of mediastinal radiation.
    - Minor risk factors (less clear significance) include:
        - Obesity
        - Sedentary lifestyle (lack of physical activity)
        - Stress
        - Excess alcohol use

CLINICAL FEATURES

- Chest pain or substernal pressure sensation;
    - Lasts less than 10 to 15 minutes (usually 1 to 5 minutes).

  - Frightening chest discomfort, usually described as heaviness, pressure. squeezing, tightness; rarely described as sharp or stabbing pain.
  - Pain is often gradual in onset.
  - Brought on by factors that increase myocardial oxygen demand, such as exertion, stress, or drugs.
  - Relieved with rest or nitroglycerin

DIAGNOSIS AND INVESTIGATION

- Note that physical examination in most patients with CCS is normal.
- Resting ECG:
  - Usually normal in patients with chronic coronary syndrome
  - Q waves are consistent with a prior MI
  - If ST-segment or T-wave abnormalities are present during an episode of chest pain, then treat as unstable angina.
- Stress test: useful for patients with an intermediate pretest probability of CAD based upon age, gender, and symptoms. Stress testing is used in the following situations:
  - To confirm diagnosis of angina
  - To evaluate response to therapy in patients with documented CCS
  - To identify patients with CCS who may have a high risk of acute coronary events
- Confirmatory tests are not routinely available at General Hospitals.
  - Refer patients who need further work up

TREATMENT

- Risk factor modification
  - Smoking cessation
  - Blood pressure control: Refer Hypertension protocol

- Dyslipidemia management: Refer Dyslipidemia protocol
- Obesity: weight loss modifies other risk factors (diabetes, HTN, and hyperlipidemia) and provides other health benefits.
- Exercise: it minimizes emotional stress, promotes weight loss, and helps reduce other risk factors.
- Diet: Reduce intake of saturated fat and cholesterol

STANDARD OF CARE FOR PATIENTS WITH CCS

- **Antiplatelet therapy**
  - ASA 75-100 mg PO daily
  - Alternative: Clopidogrel 75 mg Po daily
- **Beta blocker:** chest pain, heart rate and blood pressure control
  - **Metoprolol succinate** 50-200 mg PO daily
  - Alternative: Bisoprolol 2.5-10 mg PO daily
- **Statin**: Target LDL< 70 mg/dl, dose of statin titrated as per the response
  - **Atorvastatin** 20-80 mg PO daily
  - Alternative: Rosuva**statin** 5-20 mg PO daily
- **Angina management**
  - **Betablockers**: see above
  - Calcium channel **blockers**
    - **Amlodipine** 2.5-10 mg PO daily for those with hypertension
  - **Nitrates**
    - **Nitroglycerine** 0.4 mg sublingual tablets for acute relief
    - Isosorbid di nitrate 2.5-20 mg PO single dose or divided doses as needed
  - **Trimetazidine** 35 mg Po daily

- Review risk factor, symptoms and indication for revascularization
    - Refractory cases: Refer patients for Cardiologist evaluation

4.4.2 ACUTE CORONARY SYNDROME (ACS)

BRIEF DESCRIPTION

- ACS describes a group of clinical entities that are characterized by severe, acute myocardial ischemia or infarction resulting from thrombotic occlusion of coronary artery/ies as a result atherosclerotic plaque erosion/ rupture. Rarely, the ischemia could be due to coronary artery spasm. ACS is a medical emergency and should be managed in the intensive care unit.
- ACS comprises unstable angina, and **Acute Myocardial Infarction (**ST elevated myocardial infarction and non-ST elevated myocardial infarction).

4.4.2.1 UNSTABLE ANGINA

- Symptoms of myocardial ischemia (typical or atypical) but no elevation in cardiac enzymes, with or without ECG changes indicative of ischemia.
- Unstable angina is considered to be present in the following circumstances:
- Rest angina >20 minutes in duration
- New onset angina
- Increasing angina- more frequent or longer in duration, or occurs with less exertion than previous angina
- The following patients may be said to have unstable angina:
    - Patients with chronic angina with increasing frequency, duration, or intensity of chest pain.
    - Patients with new-onset angina that is severe and worsening.
    - Patients with angina at rest
- The distinction between unstable angina and NSTEMI is based entirely

on cardiac enzymes. The latter has elevation of troponin or creatine kinase-MB (CK-MB). Both unstable angina and NSTEMI lack ST-segment elevations and pathologic Q waves.

- Unstable angina has a higher risk of MI and death than stable angina, and patients with this diagnosis should be hospitalized.
- Its management is encompassed in Acute Coronary Syndrome.

DIAGNOSIS

- Perform a diagnostic workup to exclude MI in all patients.
- Patients with unstable angina have a higher risk of adverse events during stress testing.
- These patients should be stabilized with medical management before referral for stress testing.

TREATMENT

- Hospital admission with continuous cardiac monitoring.
- Establish IV access.
- Give supplemental oxygen if patients are hypoxic (Spo2 <90 %).
- Provide pain control:
    - **Nitroglycerin**: short acting (sublingual or spray): don't give nitrates for patients who took phosphodiesterase inhibitors (sildenafil)
    - **Morphine** 4 mg IV if pain refractory to nitrate therapy alone.
- Aggressive medical management is indicated: treat as in MI
    - Dual antiplatelet therapy:
        - **ASA** 300 mg loading followed by 81-100 mg Po daily AND
        - **Clopidogrel** 300 mg loading followed by 75 mg Po daily
    - **β-Blockers**:
    - **Metoprolol 12.5** mg Po BID and titrate as needed

- Anticoagulation using **Heparin** for the first five days until ambulation starts
    - **Enoxaparin** 1 mg/kg SC BID
    - Alternative: **Unfractionated Heparin** 5000 IU IV loading followed by 17,500 IU SC BID
- High intensity statin therapy
    - **Atorvastatin** 80 mg PO daily

AFTER THE ACUTE TREATMENT

- Refer to the next referral facility for further evaluation and treatment optimization.

4.4.2.2 ACUTE MYOCARDIAL INFARCTION (STEMI AND NSTEMI)

BRIEF DESCRIPTION

- MI is due to necrosis of myocardium as a result of an interruption of blood supply (after a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis).
- Most cases are due to acute coronary thrombosis: Atheromatous plaque ruptures into the vessel lumen, and thrombus forms on top of this lesion, which causes occlusion of the vessel.
- ST-segment elevation myocardial infarction (STEMI): Significant ST elevation or new left bundle branch block (LBBB) on ECG, elevated cardiac enzymes (Troponin and/or CKMB) and symptoms of myocardial ischemia (typical or atypical).
- Non-ST-segment elevation myocardial infarction (NSTEMI): No ST elevation on ECG (other ECG evidence of ischemia may or may not be present), elevated cardiac enzymes and symptoms of myocardial ischemia (typical or atypical).

CLINICAL FEATURES

- Chest pain
  - Intense substernal pressure sensation; often described as "crushing" and "an elephant standing on my chest."
  - Radiation to neck, jaw, arms, or back, commonly to the left side.
  - Pain is more severe and lasts longer.
  - Some patients may have epigastric discomfort.
- *Can be asymptomatic in up to one-third of patients;* painless infarcts or atypical presentations more likely in postoperative patients, the elderly, diabetic patients, and women.
- Other symptoms
  - Dyspnea
  - Diaphoresis
  - Weakness, fatigue
  - Nausea and vomiting
  - Sense of impending doom
  - Syncope
  - Sudden cardiac death—usually due to ventricular fibrillation (VFib)
- The combination of substernal chest pain persisting for longer than 30 minutes and diaphoresis strongly suggests acute MI.
- Right ventricular infarct will present with inferior ECG changes, hypotension, elevated jugular venous pressure, hepatomegaly, and clear lungs.

DIAGNOSIS

- ECG: Markers for ischemia/infarction include:
  - **Peaked T waves:** Occur very early and may be missed

  - **ST-segment elevation:** indicates transmural injury and can be diagnostic of an acute infarct.
  - **Q waves:** Evidence for necrosis (specific).
  - **T-wave** inversion is sensitive but not specific
  - **ST-segment depression:** Subendocardial injury
- **Cardiac enzymes**: currently the diagnostic gold standard for myocardial injury
  - Troponins (Troponin I and T): most important enzyme test to order
  - CK-MB: less commonly used
  - Cardiac enzymes are drawn serially: once on admission and every 6 hours until three samples are obtained.
  - The higher the peak and the longer enzyme levels remain elevated, the more severe the myocardial injury and the worse the prognosis.
- **Cardiac Monitoring for a Patient with an Acute MI**
  - BP and HR
  - Rhythm strip with continuous cardiac monitor: Watch for arrhythmias.
  - Auscultate the heart (third and fourth heart sounds, friction rub, and so on) and lungs (crackles may indicate LV failure, pulmonary edema).

TREATMENT

- Early referral to the next level facility OR urgent specialist consultation
- Give ASA 300 mg PO: Advice to chew the tablet

4.4.2.3 PERIPHERAL ARTERIAL DISEASE (CHRONIC ARTERIAL INSUFFICIENCY)

BRIEF DESCRIPTION

- Peripheral arterial disease (PAD) is an occlusive atherosclerotic disease of the lower extremities.
- Patients with PAD usually have coexisting CAD (with CHF, history of MI, and so on) and other chronic medical problems (e.g., diabetes, lung disease)
- Sites of occlusion/stenosis:
    - Superficial femoral artery (in Hunter canal) is the most common site
    - Popliteal artery
    - Aortoiliac occlusive disease

RISK FACTORS

- Smoking is by far the most important risk factor
- Chronic Coronary Syndrome
- Dyslipidemia
- Hypertension
- Diabetes: prevalence is markedly increased in these patients

CLINICAL FEATURES

- Symptoms:
    - Intermittent claudication: Cramping leg pain that is reliably reproduced by same walking distance (distance is very constant and reproducible). Pain is completely relieved by rest.
    - Rest pain (continuous): Usually felt over the distal metatarsals, where the arteries are the smallest. Often prominent at night *(awakens patient from sleep)*. Hanging the foot over side of the bed or standing

relieves pain (extra perfusion to ischemic areas due to gravity)

    - Rest pain is always worrisome: suggests severe ischemia such that frank gangrene of involved limb may occur in the absence of intervention.

- **Signs**:
    - Diminished or absent pulses, muscular atrophy, decreased hair growth, thick toenails, and decreased skin temperature
    - Ischemic ulceration (usually on the toes)
    - Localized skin necrosis: Secondary to local trauma that does not heal (due to ischemic limb)
    - Tissue infarction/gangrene in end-stage disease
    - Pallor of elevation and rubor of dependency (in advanced disease)
    - Femoral or popliteal disease causes calf claudication.
    - Aortoiliac occlusive disease causes buttock and hip claudication (in addition to the calves).

DIAGNOSIS

- Clinical suspicion based on symptoms, signs and risk factors
- Ankle-to-brachial index (ABI): Ratio of the systolic BP at the ankle to the systolic BP at the arm.
    - Normal ABI is between 0.9 and 1.3
    - ABI >1.3 is due to noncompressible vessels and indicates severe disease
    - Claudication usually when ABI <0.7
    - Rest pain usually when ABI <0.4
- Doppler study of the peripheral vessels
- Arteriography (contrast in vessels and radiographs)

  - Gold standard for diagnosing and locating PAD

TREATMENT

NON PHARMACOLOGIC

- Conservative management for intermittent claudication.
  - **Smoking cessation (the importance of this cannot be overemphasized).**
    - Smoking is linked to progression of atherosclerosis and causes vasoconstriction (further decreasing blood flow).
  - Graduated exercise program: Walk to point of claudication, rest, and then continue walking for another cycle.
  - Foot care (especially important in diabetic patients).
  - Avoid extremes of temperature (especially extreme cold).

PHARMACOLOGIC

- Atherosclerotic risk factor reduction (control of hyperlipidemia, Hypertension, Diabetes): *see specific protocols*
- **Antiplatelets**
  - **ASA** 81-100 mg Po daily
  - Alternative: **Clopidogrel** 75 mg Po daily
- **Statin**
  - Atorvastatin 20-80 mg Po daily
  - Alternative: Rosuvastatin 5-20 mg Po daily
- Consult specialist or refer patient to the next level facility for further evaluation

4.4.2.4 ACUTE ARTERIAL OCCLUSION

BRIEF DESCRIPTION

- Acute occlusion of an artery, usually caused by embolization. The common femoral artery is the most common site of occlusion. Less commonly, in situ thrombosis is the cause.

SOURCES OF EMBOLI:

- Heart (85%)
    - Atrial fibrillation is the most common cause of embolus from the heart
    - Post-MI
    - Post arterial procedure (i.e., coronary angiogram, peripheral angiogram)
    - Endocarditis
    - Myxoma
- Aneurysms
- Atheromatous plaque

CLINICAL FEATURES OF ACUTE LIMB ISCHEMIA (REMEMBER THE SIX PS)

- **P**ain: acute onset. The patient can tell you precisely when and where it happened. The pain is very severe, and the patient may have to sit down or may fall to the ground.
- Pallor
- Polar (cold)
- Paralysis
- Paresthesias
- Pulselessness

DIAGNOSIS

- Clinical: high index of suspicion with supportive clinical data.
- Doppler study of the vessels.
- ECG to look for MI, AFib
- Echocardiogram for evaluation of cardiac source of emboli—valves, thrombus, shunt

TREATMENT

- Main goal: Assess viability of tissues to salvage the limb.
- Skeletal muscle can tolerate 6 hours of ischemia; perfusion should be reestablished within this time frame.
- Immediately anticoagulate with IV heparin.
- Urgent referral to the facility where reperfusion is available in consultation with specialist.

4.5 RHEUMATIC HEART DISEASE

4.5.1 ACUTE RHEUMATIC FEVER

BRIEF DESCRIPTION

- Acute Rheumatic fever is a systemic illness in which there is inflammation of several organs.
- It occurs as non-suppurative complication of group A streptococcus pharyngitis and may consist of arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules.
- The onset of symptoms occurs 1-3 weeks after the throat infection.
- Damage to cardiac valves is the most serious complication and is usually progressive.
- In developing countries, it is a major cause of permanent damage to the heart.

- The disease occurs mainly in children of school age.
- The prevalence of rheumatic heart disease in the Ethiopian population among the asymptomatic school children is 19 per 1000 population.
- The diagnosis is based on the modified John's criteria approved by WHO in 2003. The diagnostic criteria do have major and minor manifestations.

MODIFIED JONES CRITERIA (2003)

- **Major Criteria**
    - Carditis
    - Polyarthritis
    - Chorea
    - Subcutaneous nodules
    - Erthema marginatum
- **Minor Criteria**
    - *Clinical*
        - Fever
        - Polyarthralgia
    - *Lab Tests*
    - ***Acute phase reactants***
        - Raised ESR
        - Positive C-reactive protein
        - Leukocytosis.
    - *ECG*
        - Prolonged PR interval

- **Essential Criteria**

- Documentation of recent streptococcal infection (within 45 days) is necessary for diagnosis of ARF, that is one of the following tests should be positive.

  1. Positive throat culture
  2. Raised or rising streptococcal antibody tire (Anti streptolysin O or Anti DNAse B)
  3. Rapid antigen detection tests for Group A Streptococci.

Diagnosis: requires the presence of supporting evidence for preceding streptococcal infection and the following:

1. Primary episode of Rheumatic Fever or recurrence without established rheumatic heart disease: Two major, or one major and two minor manifestations.
1. Recurrent attack of Rheumatic fever with established rheumatic heart disease-two minor manifestations.
1. Rheumatic chorea or insidious onset carditis-neither evidence of preceding streptococcal infection nor other major manifestation needed.

TREATMENT OBJECTIVES

- Eradicate streptococcal throat infection
- Prevent recurrent episodes of rheumatic fever and further valvular damage
- Treat Heart Failure, if co-existent
- Control inflammation and relive symptoms of arthritis

NON-PHARMACOLOGIC

- Bed rest if the patient has severe rheumatic carditis or arthritis/arthralgia only.
- Salt restriction if there is associated Heart Failure.

Table 4.7: Duration of secondary prophylaxis for rheumatic fever

Category of Patient	Duration of Prophylaxis
Rheumatic fever without carditis	For 5 years after the last attack or 18 years of age (whichever is longer)
Rheumatic fever with carditis with no residual valvular disease or mild mitral regurgitation	For 10 years after the last attack, or 25 years of age (whichever is longer)
Rheumatic fever with persistent valvular disease or after valve surgery	Life long

PHARMACOLOGIC

- Antibiotic (primary prevention)
- Conventional therapy for Heart Failure
- Anti-inflammatory
  - First line
    - **Aspirin,** 4-8 grams per day P.O. in 4 divided doses
    - Add a GI prophylaxis – PPI (e.g., Omeprazole 20mg, P.O., BID)
  - Alternative
    - **Prednisolone** (consider its use in severe carditis only), 1–2mg/kg per day (maximum, 80mg); only required for a few days or up to a maximum of 3 weeks.
- Prevention of recurrent rheumatic fever (secondary prevention)
  - First line
    - **Benzathine penicillin**, 1.2 million units or 600,000 units if <30 kg, every 4 weeks. It can be given every 3 weeks, to persons considered to be at particularly high risk.
  - Alternative (if penicillin allergic)
    - **Erythromycin,** 250mg, P.O. BID

Further reading

1. M Satpathy, BR Mishra. Rheumatic Fever and Rheumatic Heart Disease. JAYPEE BROTHERS MEDICAL PUBLISHERS (P) LTD. © 2013, Jaypee Brothers Medical Publishers
2. Standard treatment guideline (STG), Ethiopia. 3rd edition, 2014

4.6 VALVULAR HEART DISEASE

General description

- As a general recommendation, patients with high index of suspicion for valvular heart disease should get access for evaluation by a specialist.
- The four common valvular heart diseases are discussed below as a general guidance for management at a General Hospital level.
- Patients with acute heart failure should be managed as per the guideline.

4.6.1 MITRAL STENOSIS

- Almost all cases of mitral stenosis are due to rheumatic heart disease. Patients are usually asymptomatic until the mitral valve area is reduced to approximately 1.5 cm2 (normal valve area is 4 to 6 cm2).The disease is more common in women.

CLINICAL FEATURES

- **Symptoms**
    - Exertional dyspnea, orthopnea, PND
    - Palpitations
    - Hemoptysis
    - Thromboembolism: often associated with AFib
    - If RV failure occurs, ascites and edema may develop
- **Signs**
    - Mitral stenosis murmur.

  - With long-standing disease, will find signs of RVF (e.g., right ventricular heave, JVD, hepatomegaly, ascites) and/or pulmonary HTN (loud P2).
  - All signs and symptoms will increase with exercise and during pregnancy.

DIAGNOSIS

- CXR: Left atrial enlargement (early)
- Echocardiogram—most important test in confirming diagnosis

TREATMENT

- Consult specialist OR referral to a cardiologist

AORTIC STENOSIS

- It causes obstruction to left ventricular outflow, which results in LVH. When the aortic valve area falls below 1 cm2, cardiac output fails to increase with exertion, causing angina (but may be normal at rest).
- **Causes**
  - Calcification of a congenitally abnormal bicuspid aortic valve.
  - Calcification of tricuspid aortic valve in elderly.
  - Rheumatic fever.

CLINICAL FEATURES

- **Symptoms**
  - Angina
  - Syncope—usually exertional
  - Heart failure symptoms, such as dyspnea on exertion, orthopnea, or PND
- **Signs**
  - Murmur of aortic stenosis

DIAGNOSIS

- CXR findings: Calcific aortic valve, enlarged LV/LA (late)
- ECG findings: LVH, LA abnormality
- Echocardiography: Valve lesion, degree of stenosis, LVH

TREATMENT

- Consult specialist OR referral to a cardiologist

4.6.2 AORTIC REGURGITATION

- Also called aortic insufficiency; this condition is due to inadequate closure of the aortic valve leaflets.
- For acute aortic regurgitation, mortality is particularly high without surgical repair.

CAUSES

- **Acute**
    - Infective endocarditis
    - Trauma
    - Aortic dissection
    - Iatrogenic as during a failed replacement surgery
- Chronic
    - Primary valvular: Rheumatic fever, bicuspid aortic valve, Marfan syndrome, SLE
    - Aortic root disease: Syphilitic aortitis, aortic dissection, systemic HTN

CLINICAL FEATURES

- **Symptoms**
    - Dyspnea on exertion, PND, orthopnea

  - Palpitations—worse when lying down
  - Angina
  - Cyanosis and shock in acute aortic regurgitation (medical emergency)

PHYSICAL EXAMINATION

- Widened pulse pressure—markedly increased systolic BP, with decreased diastolic BP.
- Diastolic decrescendo murmur best heard at left sternal border.
- Peripheral signs of Aortic Regurgitation

DIAGNOSIS

- CXR findings: Enlarged cardiac silhouette, dilated aorta
- ECG findings: LVH
- Echocardiogram
  - Assess LV size and function
  - Look for dilated aortic root and reversal of blood flow in aorta
  - In acute aortic regurgitation, look for early closure of mitral valve

TREATMENT

- *Consult specialist OR referral to a cardiologist*

4.6.3 MITRAL REGURGITATION

- This condition is due to inadequate closure of the mitral valve. It could be acute or chronic. Acute form is associated with much higher mortality

CAUSES

- **Acute**
  - Endocarditis (most often Staphylococcus aureus)
  - Papillary muscle rupture (from infarction) or dysfunction (from

ischemia)
  - Chordae tendineae rupture
- **Chronic**
  - Mitral valve prolapse (MVP)
  - Rheumatic fever
  - Marfan syndrome
  - Cardiomyopathy causing dilation of mitral annulus

CLINICAL FEATURES

- **Symptoms**
  - Dyspnea on exertion, PND, orthopnea
  - Palpitations
  - Pulmonary edema
- **Signs**
  - Murmur of mitral regurgitation

DIAGNOSIS

- CXR findings: Cardiomegaly, dilated LV,pulmonary edema.
- ECG: AFib
- Echocardiogram: MR; dilated LA and LV; decreased LV function.

TREATMENT

- Consult specialist OR referral to a cardiologist

4.7 INFECTIVE ENDOCARDITIS

- Infective endocarditis is defined as an infection of the endocardial surface of the heart (usually involves the cusps of the valves).
- Always suspect endocarditis in a patient with a new heart murmur and

unexplained fever or bacteremia.

CLASSIFICATIONS (ACUTE OR SUBACUTE)

- Acute endocarditis
  - Most commonly caused by Staphylococcus aureus (highly virulent).
  - Occurs on a normal heart valve.
  - If untreated, fatal in less than 6 weeks.
- Subacute endocarditis
  - Caused by less virulent organisms, such as Streptococcus viridans and Enterococcus
  - Occurs on damaged heart valves
  - If untreated, takes much longer than 6 weeks to cause death

ORGANISMS

- Native valve endocarditis
  - *Streptococcus viridans* is the most common organism in native valve endocarditis.
  - Other common organisms include:
    - *Staphylococcus* species (*Staphylococcus aureus* more commonly than *Staphylococcus epidermidis*) and *Enterococci.*
    - *Streptococcus bovis* is associated with increased risk of active colonic malignancy
    - **HACEK** group of organisms: *Haemophilus, Actinobacillus, Cardiobacterium, Eikenella,* and *Kingella.*
- Prosthetic valve endocarditis
  - Staphylococci are the most common causes of early-onset endocarditis; symptoms appear within 60 days of surgery (Staphylococcus epidermidis more commonly than Staphylococcus aureus).

  - Streptococci are the most common cause of late-onset endocarditis; symptoms appear 60 days after surgery.
- Endocarditis in IV drug users
  - Frequently presents with right-sided endocarditis.
  - Staphylococcus aureus is the most common cause.
  - Other organisms include Enterococci and Streptococci.
  - Fungi (mostly Candida) and gram-negative rods (mostly Pseudomonas) are less common causes.

DIAGNOSIS

- Duke clinical criteria (see below): Two major criteria, one major and three minor criteria, or five minor criteria are required to diagnose infective endocarditis.
- Of note, echocardiographic evidence of vegetations is not necessary to make the diagnosis as long as sufficient Duke criteria have been met.
- Treatment should be initiated if clinical suspicion is high.
- TEE is better than transthoracic echocardiography (TTE) in the diagnosis of endocarditis for especially mitral valve pathology and small aortic vegetations.
- Most patients should get TTE as an initial screening test.

DUKE CRITERIA

- **Major Criteria**
  1. Sustained bacteremia by an organism known to cause endocarditis
  2. Endocardial involvement documented by either echocardiogram (vegetation, abscess, valve perforation, prosthetic dehiscence) or clearly established new valvular regurgitation
- **Minor Criteria**
  1. Predisposing condition (abnormal valve or abnormal risk of

bacteremia)

2. Fever
3. Vascular phenomena: Septic arterial or pulmonary emboli, mycotic aneurysms, intracranial hemorrhage, Janeway lesions[a]
4. Immune phenomena: Glomerulonephritis, Osler nodes,[b] Roth spots,[c] rheumatoid factor
5. Positive blood cultures not meeting major criteria
6. **Positive echocardiogram** not meeting major criteria
    - *Note*: Definitive (i.e., highly probable) diagnosis if two major, or one major plus three minor, or five minor criteria are present.
    - [a]Janeway lesions are painless erythematous lesions on palms and soles.
    - [b]Osler nodes are painful, raised lesions of fingers, toes, or feet.
    - [c]Roth spots are oval, retinal hemorrhages with a clear, pale center.

TREATMENT

- Consult specialist
- Three sets of blood cultures should be drawn prior to initiating antibiotic therapy
- Parenteral antibiotics based on culture results for extended periods (4 to 6 weeks)
- If cultures are negative but there is high clinical suspicion, treat empirically (See table below) until the organism can be isolated.
- If patient has intracardiac devices such as pacemaker or ICD, these must be removed●.
- Early surgical intervention is warranted for patient with:

- Acute heart failure due to valvular damage.
- left-sided infective endocarditis with highly resistant organisms (including MRSA)
- Infective endocarditis complicated by heart block or intracardiac abscess.
- Persistent bacteremia or fevers lasting 5 to 7 days after antibiotic initiation.
- Recurrent infection in those with prosthetic valves.

Note: Infective endocarditis is almost always fatal if left untreated.

Table 4.8: Empiric treatment of "community acquired" Native Valve SBE

Antibiotic regimen options	Dosage and route	Duration in weeks	Comments
Ceftriaxone PLUS **Gentamicin**	2g, IV, once per day	4-6	
	3mg/kg, IV once per day OR 1mg/kg/dose, IV, TID	2	Dose should be adjusted to Creatinine clearance. Creatinine should be monitored.

Vancomycin PLUS **Gentamicin**	15mg/kg/dose, IV, BID	4	For patients with severe or immediate **beta-lactam allergy.** Do not exceed 2g per day Adjust dose to creatinine clearance.
	3mg/kg, IV once per day OR 1mg/kg/dose, IV, TID	2	See above

*Treatment should be modified based on culture and sensitivity results as well as clinical judgement of response, risk factors and expected organisms.

Table 4.9: Empiric treatment of health care–associated and IV medicine users' endocarditis

Antibiotic-regimen	**Dosage and route**	**Duration in weeks**	**Comments**
Vancomycin PLUS **Gentamicin**	15mg/kg/dose, IV, BID	4	-Do not exceed 2g per day -Adjust dose to creatinine clearance.
	3mg/kg, IV once a day OR 1mg/kg/dose, IV, TID	2	See the table above

PROPHYLAXIS

- Scope of patients who qualify for prophylaxis is much narrower than in the past.
- Must have both a qualifying cardiac indication **AND** procedure to warrant antibiotic prophylaxis.
- Qualifying cardiac indications
  - Prosthetic heart valves (including mechanical, bioprosthetic, and transcatheter valves).
  - History of infective endocarditis
  - Congenital heart disease
    - Unrepaired cyanotic congenital heart disease.
    - Repaired congenital heart disease, with prosthetic material, during first 6 months after procedure
  - Cardiac transplant with valvulopathy.
- Qualifying procedures
  - Dental procedures involving manipulation of gingival mucosa or periapical region of teeth (extractions, implants, periodontal surgery, cleaning when bleeding expected).
  - Procedures involving biopsy or incision of respiratory mucosa
  - Procedures involving infected skin or musculoskeletal tissue

FURTHER READING

- Steven Agabegi, Elizabeth Agabegi. Step-Up to Medicine. 5th edition, 2020

CHAPTER 5:

ENDOCRINE DISORDERS

5.1 DIABETES MELLITUS

BRIEF DESCRIPTION

- Diabetes mellitus describes a group of disorders which are characterized by persistently high blood glucose levels.
- Diabetes is the leading cause of cardiovascular disease, chronic kidney disease, visual loss and non-traumatic amputations worldwide.
- The classification of diabetes includes four clinical classes
    - **Type 1 diabetes-** results from cell destruction (immune mediated or idiopathic), leading to absolute insulin deficiency.
    - **Type 2 diabetes**-results from a progressive insulin secretory defect on the background of insulin resistance.
    - **Gestational diabetes mellitus** (GDM)-diabetes diagnosed during pregnancy in previously non-diabetic woman
    - Other **specific types of diabetes** e.g., genetic defects in cell function genetic defects in insulin action, diseases of the exocrine pancreas, and medicine induced

Table 5.1: Current diagnostic criteria for diabetes mellitus

Diagnostic test	Pre-diabetes	Diabetes	Remarks
Fasting blood glucose	100-125mg/dl	≥126 mg/dl	At least 2 tests needed*
Hemoglobin A1C#	5.7-6.4%	≥ 6.5%	At least 2 tests needed*

02-hour plasma glucose	140-199mg/dl	≥200mg/dl	At least 2 tests needed
Random blood glucose		≥200mg/dl	Only classic symptoms of hyperglycemia or hyperglycemic crisis
**If both fasting blood sugar and hemoglobin A1C are done initially and both are in the diabetic range, repeat test is not necessary for the diagnosis.* *# If there is significant discrepancy between HbA1C and blood glucose measurements, use the blood glucose level.*			

- The clinical course and treatment of the different types of diabetes are different; hence, classification of the type of diabetes is very important to determine therapy.
- The traditional thinking that type 2 diabetes as the disease of adults and type 1 diabetes as the disease of children is not accurate as both diseases can occur in both age groups.

CLINICAL FEATURES

- **Symptoms**
    - Asymptomatic: there are no recognizable symptoms in the majority of patients individuals with type 2 diabetes.
    - Type 1 diabetic patients tend to be much more symptomatic than type 2 diabetic patients (weight loss, polyuria, polydipsia).
    - Fatigue, unexplained weight loss
    - Large amounts of urine (polyuria) and excessive thirst (polydipsia)
    - Unexplained weight loss
    - Blurred vision
    - Recurrent skin infections
    - Recurrent itching of the vulva (candida infections)
    - Symptoms related to chronic complications can be present at initial

diagnosis in type 2 diabetic patients;

  - Numbness or pain over the lower limbs
  - Visual impairment
  - Foot abnormalities (ulcer, ischemia, deformity)
  - Body swelling

INVESTIGATIONS

- In newly diagnosed patients
  - Diagnostic tests: Fasting or random blood glucose, glycated hemoglobin (HbA1c)
  - Urine ketones
  - Urine albumin
  - Blood urea and creatinine
  - Fasting lipid profile
  - ECG (adults)
- In diagnosed patients, follow up investigations
  - Glycemic control: HbA1c, fasting plasma glucose, post prandial plasma glucose
  - Screening for complications: Urine albumin/protein, retinal screening by ophthalmologist, serum creatinine and urea.
  - Other cardiovascular risk screening: Lipid profile (if not already on statin).

DIAGNOSIS

- The diagnosis diabetes is made based on the diagnostic criteria depicted above.
- Individuals with any one of the following need screening for type 2 diabetes. If the result is normal, repeat screening every three years; but if the result

is in the prediabetes range repeat the test every year.

- o Age 45 or above
- o Overweight or obese individuals (BMI >25kg/m2)
- o Physical inactivity
- o Hypertension
- o HDL < 35mg/dl and/or triglyceride level > 250mg/dl
- o Women with history of gestational diabetes mellitus
- o Individuals with prediabetes should be tested yearly
- o First-degree relative with diabetes
- o History of atherosclerotic cardiovascular disease
- o Women with polycystic ovary syndrome.

TREATMENT

OBJECTIVES OF TREATMENT

- Relieve symptoms
- Prevent acute hyperglycemic complications
- Prevent/delay chronic complications of diabetes
- Prevent treatment-related hypoglycemia
- Achieve and maintain appropriate glycemic targets
- Ensure weight reduction in overweight and obese individuals

5.1.1 TREATMENT OF TYPE-2 DIABETES MELLITUS

NON PHARMACOLOGIC TREATMENT

A. MEDICAL NUTRITION THERAPY (MNT): GENERAL

GUIDANCE

- **Principles of nutritional therapy**
    - Focus on supporting the patient on choosing healthy eating behaviors.
    - Consider the literacy of the individual, access to food, and willingness.
    - Try to maintain the pleasure of eating as much as possible
    - Respect and address the individual preferences, cultural, and religious choices.
    - Be nonjudgmental
    - Be practical
    - Limit food choices when only supported by scientific evidences
    - Help overweight and obese individuals to decrease body weight
    - Help attain individualized glycemic, blood pressure, and lipid goals.
- **General advice**
    - Avoid refined sugars: soft drinks with sugar, or adding sugar/honey to teas/other drinks.
    - **Carbohydrate**
        - Reduce overall carbohydrate intake
        - Carbohydrate sources high in fiber and minimally processed are preferred: whole grains, non-starchy vegetables, fruits, and dairy products
        - Be encouraged to have complex carbohydrates
    - **Fat**
        - Reduce saturated fat (animal fat) intake: butter, ghee, fatty cuts of meat, cheese.
        - Reduce Trans-fat (hydrogenated oil): solidified vegetable oils

  - Mono-saturated and polyunsaturated vegetable oils are preferred

- ○ **Protein**
  - Should be left to the individual choice.
  - When there is chronic kidney disease, reduction (not stopping) protein intake.

- ○ **Sweetened beverages**
  - Individuals who have had the habit sugar added beverages, taking low-calorie or nonnutritive- beverages can serve as short-term transition. However, they should be encouraged to replace with water intake.

B.EXERCISE

- ○ Regular moderate-intensity aerobic physical activity: for at least 30 minutes at least 5 days a week (at least 150 min/week)
- ○ Encourage resistance training three times per week.

C. WEIGHT MANAGEMENT

- ○ For obese and overweight individuals
  - Eating plans (focusing on reduction of overall carbohydrate intake) and exercise

D. Stop smoking

E. Moderation of alcohol intake

- ○ A maximum one drink for women and two drinks for men.
  - - One drink is roughly equivalent to a bottle of beer, a glass of wine, or a unit of spirit.

F. Self-blood glucose monitoring (SBGM)

G. Screening for micro and macro vascular complications

PHARMACOLOGIC TREATMENT

- **Management of blood sugar**

A. Target blood glucose

- Target should be individualized.
- In young patients with recent diagnosis, without significant chronic complications, tight glycemic control should be encouraged.
- Individuals for whom less stringent (HbA1C < 8 to 8.5%) should be considered
  - History of severe hypoglycemia
  - The elderly and those limited life expectancy
  - Established cardiovascular disease
  - Advanced microvascular disease e.g., advanced chronic kidney disease
  - Significant comorbid conditions e.g., liver disease, malignancy
  - Long duration of diabetes

B. Target in most non-pregnant adults without significant comorbidities: depicted in the table below.

Table 5.2: Glycemic targets for non-pregnant adults without significant comorbidities

Table. Glycemic targets for non-pregnant adults without significant comorbidities		
	TARGET	**Remark**
Fasting capillary glucose	**100 -130mg/dl**	In young, highly motivated, well supported patients a hemoglobin A1C target <6.5% and fasting blood glucose of 80-130mg/dl can be aimed, if it can be achieved without causing recurrent hypoglycemia.
HbA1C	**<7.5%**	

Post meal capillary glucose **(1-2hr from the beginning of meal)**	**<180mg/dl**	

C. Blood glucose lowering medicines

- **First line: Metformin**
    - ○ Initial dose 500mg to 1000mg/day daily or in two divided doses with meals.
    - ○ Titrate dose **every two weeks** depending on the fasting blood sugar
    - ○ Maximum dose = **2000mg/day (1000mg BID)**
        - The major side effects of metformin are gastrointestinal intolerance: bloating, abdominal discomfort, and diarrhea. This can be reduced by gradually increasing the dose.
        - Metformin is contraindicated in patients with advanced chronic kidney disease (eGFR <30ml/min), advanced liver disease, and hypoxia.
- **Alternative to Metformin**

1. **Add on to Metformin:** If glycemic target is not achieved by metformin alone after **three months**, add either of the following.
    - ○ **Sulfonylureas**: if Metformin is contraindicated a sulfonylurea can be started
        - Glibenclamide, Glimepiride, Gliclazide

    OR

    - ○ Basal insulin
        - Basal insulin can also be started as an alternative (see for indications for starting insulin in type 2 diabetes)
2. **Initiating two oral agents at diagnosis**
    - ○ Patients with severe hyperglycemia at presentation (Fasting blood

sugar > 250mg/dl or HbA1C>10%) and prefer oral agents than insulin, need to be started on a combination of metformin and sulfonylurea.

3. Sulfonylureas

- ○ Glibenclamide (Glyburide)
    - Starting dose is 2.5-5mg/day, 30 minutes before breakfast.
    - Titrate dose slowly to maximum of 20mg/day
    - When 10mg/day is needed, divide the total dose into two, with the larger dose in the morning.
    - Avoid in the elderly and patients with renal impairment.
- ○ Glimepiride
    - Starting dose is 1-2 mg/day, 30 minutes before breakfast.
    - Titrate dose slowly to maximum of 8mg/day
- ○ Gliclazide, modified release
    - Starting dose 30mg/day
    - Titrate the dose slowly to a maximum dose 120mg/day
- ○ **The major side of sulfonylureas is hypoglycemia.**
    - Individuals should be educated about the risk, manifestations, prevention and treatment of hypoglycemia.
    - Sulfonylureas should be avoided or given at lower doses in individuals at high risk of hypoglycemia (e.g., the elderly, with significant comorbidities, history of hypoglycemia)

4. Insulin therapy in type 2 diabetes

Indications for insulin therapy

- Failure to control blood glucose with oral medicines
- Temporary use for major stress, e.g., surgery, medical illness
- Severe kidney or liver failure
- Pregnancy
- In patients difficult to distinguish type 1 from type 2 diabetes
- Ketonuria
- Unexplained weight loss accompanied by poorly controlled blood sugar
- Initial therapy for a patient presenting with very high blood sugar
  - ○ HbA1C >10% or fasting blood glucose >250 mg/dl or random glucose consistently >300 mg/d

- ○ Dosing basal insulin in type 2 diabetes
  - If started on as an add on therapy to Metformin
    - ✓ Starting dose = NPH 10 units at bed time
    - ✓ A higher dose might be started for higher blood glucose
    - ✓ Dose increment 2-4 units in 3-7 days with self-monitoring of blood sugar
  - If started as a replacement for oral agents
    - ✓ Starting dose = NPH 15 -20 units at bed time
    - ✓ A higher dose might be started for higher blood glucose
    - ✓ For doses above 20units divided in two (about 2/3 in the morning and 1/3 in the evening)
    - ✓ Dose increment 2- 4 units in 3-7 days with self-monitoring
- ○ Addition of prandial regular insulin

- Indications to start regular insulin before meal
    - ✓ If FBS is well controlled but HbA1c is above target
    - ✓ If HbA1c is above target despite increasing basal insulin to >0.5 unit/Kg/day
- Dosing prandial regular insulin
    - ✓ Starting dose of prandial insulin: Regular insulin 4units
    - ✓ Preferred time: before the largest meal of the day
    - ✓ Dose increment 1-2 units in 2-3 days with self-monitoring of the next pre-meal blood glucose

D. Other oral diabetic medications for the care of patients with type 2 diabetes mellitus.

- ○ The above recommendations on the choice of pharmacotherapy for type 2 diabetes indicate sulfonylureas or basal insulin to be the preferred add-on therapies next to metformin. This is mainly based on cost related factors.
- ○ There are other medications which have been extensively studied and demonstrated to have benefits for different groups of patients with type 2 diabetes.
- ○ For patients who can afford to buy or get access to these medications, decision on which agent to add to Metformin, combine with Metformin from the beginning or sometimes start an initial treatment should be individualized based on the following factors.
    - The need for weight loss
    - Risk of hypoglycemia in the patient
    - the presence of cardiovascular disease
    - The presence of chronic kidney disease.
- ○ The following table shows the list of the available medications at the time of publication, their mechanism of action and the preference (see the table below)

Table 5.3: Available medications and their mechanism of action and the preference

Class of medication	Available drugs and formulations in Ethiopia	Mechanism of glucose lowering	Clinical sates in which the drug is most beneficial	Common side effects
SGLT2 inhibitors (Sodium glucose transporter -2 inhibitors)	**Dapagliflozin** 10mg or 5mg tablet Dosage: 5 or 10mg, po, once daily	Increased urinary glucose excretion by the kidneys	• Heart failure • Early stages of CKD • Compelling need to decrease the risk hypoglycemia • Compelling need to decrease weight loss or reduce weight • Need to improve glycemic control Additional benefit of BP lowering	• Increased urination • Vulvovaginal fungal infections and UTI • Might increase the risk of DKA Avoid in advanced CKD

DPP4-inhibitors (Dipeptidyl peptidase -4 inhibitors)	**Saxagliptin** 2.5 or 5mg (also, as fixed drug combination with Metformin 500mg or 1000mg) Dosage: 2.5 -5mg, po, once daily **Vildagliptin** 50mg (also, as fixed drug combination with Metformin 500mg or 1000mg) Dosage: 50mg, po, once daily or BID	• Inhibition of DPP-4 enzyme, increase the level of incretins. • Increases glucose-dependent insulin secretion. Reduce glucose release from liver after meals	• Compelling need to decrease the risk hypoglycemia • Need for intensification of glycemic control • Weight neutral (no increment or significant decrement)	• Upper respiratory tract infections • Headache Dose reduction need in patients with CKD.

E. Management of other cardiovascular (CV)risks

- **Cardiovascular risk calculation**
  - All patients 10-year cardiovascular risk factor needs to be calculated (see section on ischemic heart disease)
- **Blood pressure management** (See section on hypertension)
  - Target blood pressure: <130/80mmHg

- First line if there is proteinuria: ACE inhibitors or ARBs
- First line if no proteinuria: Calcium channel blocker, thiazide diuretics or ACE inhibitors or ARBs.
- Preferred two drug combinations for patients with proteinuria
  - ✓ ACE inhibitors/ARB + Calcium channel blockers
  - ✓ ACE inhibitors/ARB + Thiazide diuretics
- Preferred combination for patients with no proteinuria
  - ✓ Calcium channel blockers + ACE inhibitors/ARB
  - ✓ Calcium channel blockers + Thiazide diuretics
- Preferred three drug combinations
  - ✓ ACE inhibitors/ARB + calcium channel blockers + Thiazide diuretic

- ○ **Lipid lowering therapy**
  - **Indications**
    1. Age above 40 without additional CV risk
       - Start moderate intensity statin
       - Make it high intensity if there is additional CV risk
    2. All ages with a history of cardiovascular risk
       - Start high intensity statin
    3. Age 20-39 years with one or more CV risk factor
- ○ **Antiplatelet therapy**
  - **Aspirin (81-162mg/day)**
    - It is only indicated for patients who have CV disease (coronary artery disease, ischemic stroke or peripheral arterial disease)

5.1.2 TREATMENT OF TYPE 1 DIABETES MELLITUS_

NON PHARMACOLOGIC TREATMENT

- See in the management type 2 Diabetes

PHARMACOLOGIC

- Insulin is the main stay of treatment in type 1 diabetes
- Insulin regimen in type 1 Diabetes Mellitus:
  - **Conventional insulin therapy**
    - It encompasses simpler non-physiologic insulin regimens.
    - These include single daily injections, or two injections per day (including a combination short-acting and -NPH insulin)
  - **Intensive insulin therapy**
    - It describes treatment with >3 injections/day or continuous insulin infusion
    - It requires frequent monitoring of blood sugar: fasting, before lunch, before dinner & before bed.
    - It also requires the following
      - ✓ Counting and recording carbohydrates.
      - ✓ Adjusting insulin doses in response to given glucose patterns.
      - ✓ Coordinating diet, exercise, and insulin therapy.
      - ✓ Responding appropriately to hypoglycemia
  - **Designing insulin therapy**
    - Total insulin dose per day Initiation, 0.2 to 0.4 units/kg/day
    - Maintenance – highly variable roughly 0.6 to 0.7 units/kg/day

- – Regimen options-with NPH and regular insulin

A. **Preferred regimen: NPH with premeal regular insulin**

- o NPH before breakfast and at bed time

  PLUS

- o Regular Insulin three times daily injection: before breakfast, lunch, and dinner

A. **Other options:** If the patient work, routines, social circumstances, and support do not allow the patient to do the preferred regimen

- o NPH with pre-breakfast and pre-dinner regular insulin
- o Mixed NPH and regular insulin -70/30 (70% NPH & 30% regular)
- o Twice daily NPH injections only: Before breakfast and before bedtime

5.1.3 DIABETIC KETOACIDOSIS (DKA) AND HYPERGLYCEMIC HYPEROSMOLAR STATE (HHS)

BRIEF DESCRIPTION

- Diabetic ketoacidosis (DKA) is a condition in which there is a severe deficiency of insulin resulting in very high blood glucose.
- Fat is broken down as an alternative source of energy with ketones/ ketoacids as a by-product.
- This state of severe hyperglycemia and ketone body production results in severe metabolic, fluid and electrolyte abnormalities.
- DKA often occurs in type 1 diabetes patients but may also occur in type 2 diabetes.
- The most common settings in which DKA occurs include:
  - o Previously undiagnosed and untreated diabetes

- Interruption therapy
- Stress of inter-current illness (e.g., infection, myocardial infarction, stroke, surgery, complicated pregnancy etc.)

- Hyperglycemic hyperosmolar state (HHS) is a hyperglycemic emergency that occurs in type 2 DM due to relative insulin deficiency and inadequate fluid intake.
- Apart from acidosis the manifestations, risk factors and management of HHS is similar to DKA

CLINICAL FEATURES

- **Symptoms**
  - Excessive urination
  - Excessive thirst and drinking of water
  - Nausea, vomiting
  - Abdominal pain
  - Symptoms of infection or other precipitants
- **Signs**
  - Deep and fast breathing
  - Low blood pressure
  - Fast and weak pulse
  - Alteration in sensorium or collapse
  - Dehydration with dry skin, reduced skin turgor or sunken eyes
  - Fruity' breath (smell of acetone) in DKA
  - Evidence of infection, recent surgery, stroke etc.

INVESTIGATIONS AND DIAGNOSIS

- **Investigations**

  - Random blood glucose: usually >300mg/dl)
  - Urine glucose (usually >3+)
  - Urine ketones (usually >2+)
  - BUN and Creatinine
  - Serum electrolytes, particularly serum potassium
  - Investigations for precipitants: CBC, blood film for malaria parasites and others based on the suspected precipitating factors

- **Diagnosis**
  - Diagnosis of DKA or HHS is made with the presence of severe hyperglycemia, clinical features and ketone in the urine (in case of DKA)
  - Sometimes DKA can occur in relatively lower blood sugar (euglycemic DKA)

TREATMENT

OBJECTIVES OF TREATMENT

- Replace fluid losses
- Replace electrolyte losses and restore acid-base balance
- Replace deficient insulin
- Seek the precipitating cause and treat appropriately

NON-PHARMACOLOGIC

- Admit to intensive care unit (or a ward patient can be very closely observed)
- Closely monitor fluid input and urine output

PHARMACOLOGIC

- Replace **fluids:** Individualize fluid needs based on the patient hydration status; the following is a guide to severely dehydrated patients.
  - **Initial fluid**

    - 1000ml NS the first hour.
    - Reassess for hydration status: if still severely dehydrated, give another 1000ml NS over the next 01 hour.
  - **Subsequent fluid**
    - Depends on the hydration status and urine output of the patient.
    - On average give about 250 mL/hour (1000ml over 04 hour) in the first 24 hours or until patient is able to take enough oral fluids.
    - Reassess the patient hydration status to decide subsequent Iv fluid needs.
  - **Changing fluid**
    - Change the NS to 5% DW9D when plasma glucose reaches 250 mg/dl in DKA and 300mg/dl in HHS.
  - HHS requires more fluid.
  - Assess hydration status, BP and urine output frequently.
  - In patients with impaired kidney function and cardiac disease more frequent monitoring must be performed to avoid iatrogenic fluid overload.
- Administer **short-acting insulin**
  - **Regular Insulin**
    - 10units IV- and 10-units IM, stat,

Then

    - If there is perfuser: 0.1units/kg per hour by continuous IV infusion.
    - If there is no perfuser: 5 units, I.M, every hour.
  - **Goal**

    - Reduce serum glucose by 50 to 70 mg/dl in the 2-3 hours
    - If the drop is <50mg/dl in 2-3 hours, double the regular insulin.
    - If the drop is faster, reduce the dose by half for continuous infusion and give the IM insulin every 2 hour.

- **Potassium**
  - All patients with DKA have potassium depletion irrespective of the serum K+ level.
    - If the initial serum K+ is <3.3 mmol/l, do not administer insulin until the K is corrected.
    - If the initial serum K + is >5.3 mmol/l, do not supplement K until the level reaches < 5.3.
    - If K+ determination is not possible delay initiation of K replacement until there is a reasonable urine put (>50 ml/hr)
  - Add intravenous KCl in the IV fluids
    - Add 40–60 mmol/l of IV fluid when serum K+ < 3.7 mmol/l
    - Add 20-40 mmol/l of IV fluid when serum K+ < 3.8-5.2 mmol/l
  - The serum potassium should be maintained between 4.0 and 5.0 mmol/l

- **Precipitant identification and treatment**
  - Noncompliance, infection, trauma, infarction. Initiate appropriate workup for precipitating event (cultures, CXR, ECG)
- **Follow up of response**
  - Blood glucose every 1–2hrs
  - Urine ketones every 4hr
  - Electrolytes (especially K+) every 6 h for first 24 h.
- **Continuation of treatment**

  - ○ The above treatment should continue until the patient is stable, clinically acidosis improves, and patient is able to take oral feeding.
  - ○ The urine ketone might still be positive, as it usually lags behind the improvement of acidosis.
- **Transition**
  - ○ Once the patient is able to take oral feeding and clinically the acidosis improved.
    - – **Reduce regular insulin**: 2-3 units hourly (5 units every 2 hour) or for continuous infusion by 0.05/kg per hour
    - – **Overlap** regular insulin with subcutaneous NPH insulin for 2-3 hours
    - – **NPH insulin dosing**
      - ✓ If previously on insulin: start the pre DKA or pre-HHS dose
      - ✓ If Insulin naïve: 80% of the 24-hour requirement or 0.5 to 0.8kg/day (divided in to basal and bolus)

5.1.4 HYPOGLYCEMIA IN DIABETES

BRIEF DESCRIPTION

- Hypoglycemia is a blood sugar level low enough to cause symptoms and signs.
- It is a common complication of glucose lowering therapy in diabetes.
- Sulfonylureas and insulin are the most common causes of hypoglycemia.
- The elderly, patients with impaired kidney function and multiple comorbidities are at higher risk of hypoglycemia.
- A value <70mg/dl is agreed as alert level to define hypoglycemia in diabetes.

- It should be remembered some patients might be symptomatic at levels>70mg/dl and some might not develop symptoms at level <70mg/dl.
- Pseudo hypoglycemia is an event during which the person with diabetes reports typical symptoms of hypoglycemia but with a measured blood glucose concentration >70 mg/dl.These patients commonly have chronically high blood sugar and they experience symptoms of hypoglycemia at plasma glucose levels >70 mg/dl **as glucose levels starts to improve.**
- Whipple's **triad** is a combination of three essential elements useful for the diagnosis of hypoglycemia in general.
  - Symptoms and signs of hypoglycemia
  - Documented low blood glucose level
  - Relief of symptoms up on correction of the low blood glucose.
- **Hypoglycemia unawareness** is a situation where symptoms of hypoglycemia are not felt by the patient in spite of having low blood glucose levels. It is a common and challenging problem is patients with long standing diabetes.

CLINICAL FEATURES

- The symptoms of hypoglycemia are classified in to adrenergic and neuroglycopenic

Adrenergic(autonomic)	Neuroglycopenic (brain glucose deprivation)
• Palpitation • Tremor • Anxiety • Hunger • Sweating • Tingling	• Difficulty concentrating • Difficulty in speaking • Blurred vision • Incoordination • Confusion • Loss of consciousness • Seizure

- Asymptomatic: diabetic patients with hypoglycemia can be asymptomatic; this hypoglycemia unawareness results from autonomic dysfunction.

INVESTIGATIONS

- Glycemia related: FBS, postprandial blood sugar and HbA1c
- Creatinine and urea

DIAGNOSIS

- The diagnosis of hypoglycemia is diabetes is made with either of the following
  - A documented blood glucose level <70mg/dl

    OR

  - Presence of symptoms which improve with treatment
- Classification of diabetes associated hypoglycemia based on severity

Level 1	Blood glucose 54-70 mg/dl
Level 2	Blood glucose <54 mg/dl
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia

TREATMENT

OBJECTIVES OF TREATMENT

- Reverse hypoglycemic symptoms
- Prevent brain damage
- Prevent recurrence

NON-PHARMACOLOGIC

- The main stay of management of level 1-2 (mild to moderate) and level-3 (severe) hypoglycemia with preserved consciousness taking or providing glucose rich food/drinks(sweets).

- Pure glucose is preferred but any carbohydrate rich food can be used
    - Give 04 teas spoon of sugar diluted in water
    - Monitor blood sugar every 20-30 minutes
    - If no improvement, repeat the above
    - Once blood sugar improves, the patient must take a meal or snack
- Alternatives: regular soft drinks
    - 200ml of Mirinda® or Cola® contains about 20gram sugar can replace the above.
- Avoid protein rich foods as they increase insulin response

- For hypoglycemia unawareness: a 2-3 weeks period of avoiding hypoglycemia through frequent self-monitoring of blood glucose and keeping the blood glucose at higher levels may restore awareness.

PHARMACOLOGIC

- In patients who present to health facilities with decreased level of consciousness from severe hypoglycemia
    - 40% Dextrose (20ml vial)
        - Give 03 vials IV, fast
        - Monitor blood sugar every 20-30 minutes
        - If blood sugar is <70mg/dl, give another 03 vials of 40% dextrose and start 5-10% dextrose infusion. Continue to monitor blood sugar every 20-30 minutes.
        - When the patient can take orally give regular meal or snack. .

PREVENTION OF HYPOGLYCEMIA IN DIABETICS

- Self-monitoring of blood sugar
- Patient, family/care giver education

- ○ A standardized education on rigorous avoidance of hypoglycemia
- ○ On conditions which increase the risk of hypoglycemia
  - – Fasting or delayed meals
  - – Consumption of alcohol
  - – Intense exercise
- ○ Symptoms of hypoglycemia and possibility of hypoglycemia unawareness
- ○ Treatment of hypoglycemia at earliest warning symptoms or at <70mg/dl
- ○ Adjusting glycemic targets to higher levels, if hypoglycemia is recurrent
- ○ Reporting episodes of hypoglycemia to physician

5.1.5 CHRONIC COMPLICATIONS OF DIABETES

Brief description

- The complications of diabetes are classified in two major groups
  1. Microvascular: Diabetic kidney disease, retinopathy and nephropathy
  2. Macrovascular: coronary artery disease, stroke and peripheral vascular disease
- Diabetic foot disease is also a major complication which results from multifactorial causes
- Prevention, detection, delaying progression and supportive management of these complications is an important part of care of patients with diabetes
- Prevention of these complications can be achieved through optimal glycemic control, optimal blood pressure management, lipid control, quitting smoking and maintaining a healthy life style.

- Screening, follow up, prevention and treatment of the microvascular complications is summarized in the table below

Table 5.4: screening and management of chronic complication of diabetes

Complications	Initial screening	Follow up screening	Prevention& Treatment
Nephropathy	• T1DM-after 5 years • T2DM - at diagnosis • Screening tool: - Albuminuria - Creatinine, eGFR	• No nephropathy -annually • Nephropathy- 2x/yr • Refer if eGFR <30ml/min	• Optimize glycemic control • Optimize BP control • ACEi/ARB for proteinuria
Retinopathy	• T1DM-after 5 years • T2DM – at diagnosis • Before and at time of pregnancy • Screening tool: - Dilated eye examination by ophthalmologist	• No retinopathy-in 1-2yr • Retinopathy-1yr • Sight threatening retinopathy - more frequent evaluation	• Optimize glycemic control • Optimize BP control • Optimize lipid control • Pan retinal laser photocoagulation • Intravitreous injections of anti– vascular endothelial growth • ASA is not in patients with retinopathy

Neuropathy	• T1DM-after 5 years • T2DM – at diagnosis Screening tool • Careful history • Temperature/ pin-prick & vibration sensation • 10-g monofilament testing	Annually	• Optimize glycemic control • Symptomatic management • Painful neuropathy o Amitriptyline: 12.5-50mg PO/bedtime • Gastroparesis o Metoclopromide 10mg PO, TID(syrup preferred) Alternatives (2nd line) o Domperidone 10mg PO TID o Erythromycin syrup, 50-250mg, TID • Diabetic diarrhea o Symptomatic treatment Loperamide 2-4mg, PO, 6-8hrly or Codeine 30mg, PO,6-8hrly o Treatment of bacterial overgrowth: Antibiotics 7-10days Norfloxacin 400mg, BID Or Metronidazole500mg TID + Cephalexin 500mg TID/or Cotrioxazole 960mg BID • Postural hypotension o Change posture slowly o Elevate head by 10-20^{0} o Dorsiflexion of feet and handgrip (before standing o Tensing legs by crossing (when standing) • Bladder dysfunction o Remove drugs which worsen it (Amitriptyline, calcium channel blockers) o Strict voluntary voiding schedule o Crede maneuver (lower abdominal pressure by hands) o If severe: Self intermittent catheterization • Erectile dysfunction Use PDE5 inhibitors - Take 01hr before sexual encounter - On empty stomach - Avoid use with nitrates o Sidenafil 25-100mg (start with 50mg o Vardanfil 10-20mg o Tadalafil 10-20mg If refractory o Tadalafil2.5-5mg/daily

Diabetic foot	Initial visit Screening tools - Assessment of skin & foot deformities - Neurologic exam - Peripheral arterial disease evaluation	Every visit	• Optimize glycemic control • Stop smoking • Pain management in painful peripheral neuropathy • Education on foot care • Specialized therapeutic foot ware for patients with callous deformities, ulcers, or amputation

Further reading

1. American Diabetes Association Standards of Medical care in diabetes—2020.
2. International Diabetes Federation. Recommendations For Managing Type 2 Diabetes In Primary Care, 2017. www.idf.org/managing-type2-diabetes
3. Mohan, V., Khunti, K., Chan, S.P. *et al.* Management of Type 2 Diabetes in Developing Countries: Balancing Optimal Glycaemic Control and Outcomes with Affordability and Accessibility to Treatment. *Diabetes Ther.* 2020. 11, 15–35

5.2 DYSLIPIDEMIA AND METABOLIC SYNDROME

BRIEF DESCRIPTIONS

A. METABOLIC SYNDROME

- The metabolic syndrome is defined as the co-occurrence of risk factors for atherosclerotic cardiovascular disease (ASCVD) and future development of type 2 diabetes.
- Abdominal obesity and the associated insulin resistance are considered to be main pathogenic mechanism behind the metabolic syndrome.
- The most important clinical implication of diagnosing metabolic syndrome is intensification of life style and pharmacologic based ASCVD risk reduction.

B. DYSLIPIDEMIA

- Dyslipidemias are disorders of lipoprotein metabolism that may result in the following abnormalities: High total cholesterol (TC), high low-density lipoprotein cholesterol (LDL-C), high non-high-density lipoprotein cholesterol (HDL-C), high triglycerides (TG), or low HDL-C.
- Serum cholesterol and its lipoprotein carriers (LDL, and VLDL) are known to be related to atherosclerotic cardiovascular disease (ASCVD).
- LDL-cholesterol is the dominant form of atherogenic cholesterol.
- HDL-cholesterol is not atherogenic.
- Although LDL-Cholesterol is a primary cause of atherosclerosis, other major cardiovascular risk factors contribute a lot.
- The major cardiovascular risk factors include cigarette smoking, hypertension, diabetes, other non-LDL abnormalities and old age
- LDL-C is calculated with the formula: LDL= Total-cholesterol– (triglycerides/5) – HDL. When triglyceride level is above 400mg/dl, this equation is sufficiently accurate.

C. ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) RISK CALCULATION AND PREVENTION

- Coronary artery disease, ischemic stroke, and peripheral arterial disease the major atherosclerotic cardiovascular diseases (ASCVD)
- Primary prevention of ASCVD is a preventive strategy implemented in individuals at increased risk before the development of the ASCVD.
- Secondary prevention is a preventive strategy implemented in individuals who have past or current ASCVD.
- ASCVD risk calculation tools are validated tools of predicating the probability of developing these diseases in the future, generally expressed as the percentage probability in the coming 10 years.
- Decision on treatment and intensity of treatment of dyslipidemia for primary prevention should be based on the calculated ASCVD risk.

CLINICAL FEATURES

- Central obesity
- High blood pressure
- Xanthelasmas and xanthomas
- If ASCVD has already developed: angina pain, intermittent claudication, transient ischemic attacks

DIAGNOSIS AND INVESTIGATIONS

- The diagnosis of metabolic syndrome is based on the presence of three of the following five risk factors;

Table 5.5: criteria for the diagnosis of metabolic syndrome

No	Risk factor	Defining level
	Waist circumference	Men >102 cm Women > 88 cm
	Triglycerides	>150 mg/dl
1.	HDL cholesterol	Men <40 mg/dl Women <50mg/dl
2.	Blood pressure	130/85 mm Hg
	Fasting glucose	>100 mg/dl

- For calculation of ASCVD risk use the AHA/ACC 2013 ASCVD Risk Calculator which available as freely downloadable tools for smartphones or online use.
- After calculating the 10yr ASCVD, categorize individuals in the age 40-75year in to the following risk categories.

<5% = LOW RISK

5 to < 7.5% = BORDERLINE

7.5 to< 20% = INTERMEDIATE

>20% = HIGH

- The presence of CKD, metabolic syndrome, inflammatory diseases like rheumatoid arthritis and HIV, premature menopause, family history of premature ASCVD increase the risk and are considered das risk modifiers.

- Additional investigations
    - FBS and HbA1C
    - Urinary protein/albumin
    - Creatinine and urea/eGFR

TREATMENT

OBJECTIVES OF TREATMENT

- Reduction of future development of ASCVD
- Prevention of early mortality

NON- PHARMACOLOGIC MANAGEMENT

- **Life-style modification**
    - **Diet**
        - Diet that emphasizes intake of vegetables, fruits, whole grains, legumes
        - Healthy protein sources (low-fat milk products), low-fat chicken (without the skin), and fish
        - Limits intake of sweets, sugar-sweetened beverages, and red meats
    - **Weight Control**
    - **Physical Activity**
        - At least 150 minutes per week (e.g., At least ½ hour 5-7x/wk) of moderate-intensity physical activity or 75 minutes of vigorous intensity.
        - Moderate intensity physical activity: typical example brisk walking
        - Vigorous intensity physical activity: typical example Jogging, running or biking

PHARMACOLOGIC TREATMENT

- **Statin therapy**
  - The intensity of statin therapy is divided into 3 categories
    1. High-intensity statin = lowers LDL-C levels by ≥50%
    2. Moderate-intensity statin = lowers LDL-C levels by 30% to 49%,
    3. Low-intensity statin therapy = lowers LDL-C levels by <30%

Table 5.6: Intensity of statin therapy

	High intensity	Moderate intensity	Low intensity
Atorvastatin	40-80mg (commonly used 40mg)	10-20mg (commonly used 20mg)	-
Rosuvastatin	20-40mg (commonly used 20mg)	5-10mg (commonly used 10mg)	-
Simvastatin	-	20-40mg	10mg
Lovastatin	-	40mg	20mg

Table 5.7: Intensity of statin therapy

Table. Indications of statin therapy

High intensity statin	Moderate intensity	Low intensity
1. Anyone with LDL-C >190mg/dl 2. Secondary prevention 3. Age 40-75yr and ASCVD risk >20% 4. DM, age 40-75yr +risk enhancers	1. Anyone with DM + age 40-75yr 2. No DM + Age 40-75 + ASCVD RISK 7.5-20% + risk enhancers 3. Age 20-39yr, LDL>160mg/dl and family history of premature ASCVD 4. If high intensity therapy is not tolerated	1. Age 40-75yr, Borderline risk (5-7.5%) + multiple risk enhancers 2. If moderate intensity therapy is not tolerated

STATIN SAFETY

- Statin therapy is usually well tolerated and safe.
- Some side effects are seen occasionally.
- The most common side effect a statin-associated muscle symptom. Myalgia is more common than genuine myositis, or the very rare rhabdomyolysis.
- If muscle symptoms are mild, another statin can be rechallenged with a lower intensity.
- Statins increase the risk of new onset diabetes modestly but it should not be reason not to start or withdraw statins.

- **Other pharmacologic treatments in metabolic syndrome**
  - Hypertension and diabetes should be treated as per the standard treatment guideline.

FURTHER READING

1. 2019 ESC/EAS Guidelines for the management of dyslipidemias: lipid modification to reduce cardiovascular risk. European Heart Journal (2020) 41, 111188.
2. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. *Circulation*. 2019;139: e1082–e1143.

5.3 THYROID DISORDERS

5.3.1 GOITER

BRIEF DESCRIPTION

- Goiter (Goitre) refers to an enlarged thyroid gland.
- The most common cause of Goiter in Ethiopia is endemic goiter, which results from iodine deficiency and/or regular the regular consumption of

goitrogenic.

- Goitrogenic foods are foods that inhibit thyroid hormone synthesis e.g., Millet, cabbage, kale etc.
- Goiter can be present with normal or abnormal thyroid function.

Causes of goiter

1. Endemic goiter (iodine deficiency and/or regular consumption goitrogenic foods)
    - Simple
    - Toxic
2. Grave's disease
3. Thyroiditis
4. Physiologic goiter (pregnancy and puberty)
5. Benign thyroid tumor (adenoma)
6. Thyroid cancer

CLINICAL FEATURES

- **Symptoms**
    - Majority of individuals with goiter do not have symptoms
    - Swelling in anterior neck
    - Disfigurement
    - Compression of symptoms from large goiter or growth behind the sternum (retrosternal goiter): hoarseness of voice, stridor, difficulty of swallowing
    - Occasional postural dizziness
    - Symptoms of hyperthyroidism or hypothyroidism (see next) may be present

- **Signs**
  - Visible or Palpable thyroid gland
  - Enlarged (engorged) neck veins
  - Signs of hyperthyroidism or hypothyroidism (see next) may be present

Table 5.8: WHO Grading of goiter size (mainly for epidemiologic purposes)

1. Grade 0: Group 0: normal thyroid, no palpable or visible goiter
2. Grade 1: A goiter that is palpable but not visible when the neck is in the normal position
3. Grade 2: A goiter that is clearly visible and palpation is when the neck is in normal position

DIAGNOSIS

- The diagnosis of goiter is based on physical examination.
- The next step two steps in the evaluation are the following;
  1. Determining thyroid function test: serum TSH (Thyroid stimulating hormone)
  2. Thyroid ultrasound
     - Ultrasound features that make thyroid nodules suspicious for malignancy:
       - Hypoechogenicity
       - Microcalcification
       - Hypervascularity
       - Irregular borders
       - Taller than wide
     - Thyroid imaging reporting and data system (TI-RADS) is a helpful ultrasound-based risk stratification system to identify thyroid

nodules with high risk for malignancy.

- TI-RADS 4b and 5 nodules need FNAC.
- TI-RADS 4a and 3 lesions may need FNAC is they are large or rapidly growing.

3. Evaluation for possible malignancy: FNAC (Fine needle aspiration biopsy)

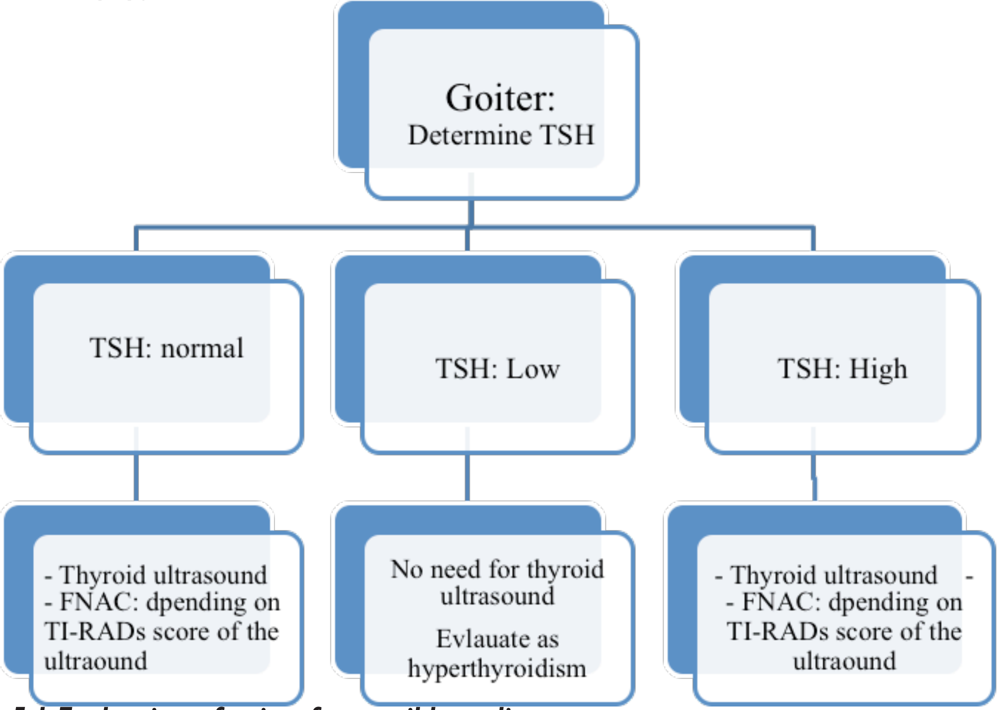

Goiter:
Determine TSH
TSH: normal
TSH: Low
TSH: High
- Thyroid ultrasound
- FNAC: dpending on TI-RADs score of the ultraound
No need for thyroid ultrasound
Evlauate as hyperthyroidism
- Thyroid ultrasound -
- FNAC: dpending on TI-RADs score of the ultraound

Fig. 5.1 Evaluation of goiter for possible malignancy

TREATMENT

OBJECTIVES OF TREATMENT

- The goal of treatment for goiter depends on clinical presentation
  - Improving physical compression symptoms: surgical treatment
  - Addressing aesthetic concerns(disfigurement): surgical treatment
  - Correcting hyperthyroidism or hypothyroidism: pharmacologic treatment

NON-PHARMACOLOGIC TREATMENT

- The main non-pharmacologic treatment of goiter is surgical management.
- The main indications for surgery (thyroidectomy) are the following;
  - Thyroid cancer
  - Compression symptoms
  - Toxic multi-nodular goiter: after correcting the thyrotoxicosis
  - Aesthetic concerns

PHARMACOLOGIC TREATMENT

- There is no specific pharmacologic treatment for decreeing the size of uninvestigated goiter.

Routine use of iodine or Lugol's solution to decrease the size of a grossly enlarged nodular goiter should be avoided.

PREVENTION

- The most common cause of goiter, endemic goiter is mainly caused by iodine deficiency.
- Correction iodine deficiency at community level is an effective strategy,
- Universal iodization of salt is the preferred method of prevention.
- In iodine deficient community to prevent the consequences of iodine deficiency in children, iodine supplementation for pregnant women, lactating women and children less than 2 years.
  - Medication for prevention:
    - **Iodized oil capsule**, strength 190 mg of iodine per capsule

Table 5.9: The recommended dosage of Iodized oil capsule

Category	Dosage
• Children less than 6 months	Exclusive breast feeding, treat the mother
• Children 6 months to 1 year	1 capsule (190 mg) once a year
• Children from 1 to 2 year	2 capsules (380 mg) once a year
• Pregnant or lactating women	2 capsules (380 mg) once a year

FURTHER READING

1. MARK A. KNOX. Thyroid nodules. American Family Physician. 2013; Volume 88, Number 3. www.aafp.org/afp
2. WHO/NHD/01.1 Assessment of Iodine Deficiency Disorders and Monitoring their Elimination, A guide for programme managers, second edition.
3. M Andersson, B de Benoist, F Delange and J Zupan. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutrition: 10(12A), 1606–1611.

5.3.2 THYROTOXICOSIS

BRIEF DESCRIPTION

- A condition resulting from an excess of thyroid hormones,
- If left untreated, significant weight loss and cardiac complications, including Heart Failure, may occur.
- Causes
    - Grave's disease (autoimmune, common in females)

- Toxic multinodular goiter
- Toxic adenoma
- Thyroiditis (causes transient thyrotoxicosis which progresses to normal or hypothyroid state later)
- Iatrogenic causes (side effect of medications containing iodine e.g. amiodarone)

CLINICAL FEATURES

- **Symptoms**
  - Weight loss despite increased appetite
  - Excessive sweating
  - Heat intolerance
  - Palpitations
  - Nervousness and irritability
  - Menstrual irregularity, mainly oligomenorrhea
  - Increased hair loss
  - In thyroiditis there could be neck pain and
- **Signs**
  - Tachycardia with or without irregularity: Sinus tachycardia or atrial fibrillation
  - High blood pressure
  - Goiter often present but not always;
    - Smooth and diffuse goiter in Grave's disease
    - Irregular goiter in toxic multi-nodular goiter
    - Single thyroid nodule in toxic adenoma
    - Thyroiditis: there could tenderness

- Tremors and brisk deep tendon reflexes
- Moist palms
- Exophthalmos (Staring or protruding eye, lid lad/retraction in Grave's disease)
- Investigations
- TSH
- Free T4, if TSH is abnormal
- ECG
- Thyroid imaging and cytology are not generally necessary in the work up of hyperthyroidism.

DIAGNOSIS

- TSH is the best initial diagnostic test.
- If the TSH is low, it suggests hyperthyroidism
- A low TSH result should be followed by Free T4 and total T3 determinations. Rarely Free T3 determination may be needed.
    - TSH normal = excludes hyperthyroidism
    - TSH is low and high Free T4 or T3 = Primary hyperthyroidism
    - If TSH is low, Free T4 and T3 normal= subclinical hyperthyroidism

TREATMENT

OBJECTIVES OF TREATMENT

- Improve symptoms
- Prevent or treat complications

NON PHARMACOLOGIC TREATMENT

- Avoid stimulants e.g., Caffeine
- Partial thyroidectomy; should only be done after a state of euthyroidism is

achieved with medical therapy

- Radioiodine therapy

PHARMACOLOGIC TREATMENT

1. **Anti-thyroid drugs**

- **First line**
  - **Carbimazole**
    - Initial dose 30-40mg/day divided in 2-3 doses
    - Maximum dose 60mg/day
    - Maintenance dose: variable but commonly 5-15mg/day
    - Titrated down the dose based on thyroid function tests:
      - In the initial few months based on Free T4 levels and T3
      - After the first few months follow up is based on TSH
- **Second line /alternative**
  - **Propylthiouracil (PTU)**
    - PTU is the first line in pregnant women
    - Initial dose: 300 - 400mg/day in 3 divided doses
    - Maximum dose 900mg/day
    - Maintenance dose: Variable but commonly 100-200mg/day
    - Agranulocytosis is a rare but serious adverse effect of PTU. It should be suspected if patients develop fever, sore throat or other features of infection
    - Hepatotoxicity is another serious adverse effect of PTU
- **Duration of treatment with anti-thyroid drugs**
  - Depends on the specific cause of the hyperthyroidism

- **In Grave**'s disease: hyperthyroidism generally resolves in 1.5 - 2 years; hence, if euthyroid state is achieved the anti-thyroid drug needs to be discontinued in 15 to 2 years.
- In toxic multinodular goiter or toxic adenoma: treatment should continue until thyroidectomy or radioiodine therapy is done

2. **Adjunct pharmacologic treatment**
   - **Beta blockers**: for symptom control until euthyroid state is achieved.
     - **Propr**anolol, 20-40mg, PO every 8-12 hours

       OR
     - Atenolol 25-100mg, PO, daily

       OR
     - Metoprolol 25-100mg, PO, daily or in two divided doses

FURTHER READING

1. Douglas S. Ross, Henry B. Burch, David S. Cooper, M. Carol Greenlee et al. American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. THYROID Volume 26, Number 10, 2016
2. Igor Kravets. Hyperthyroidism: Diagnosis and Treatment. American Family Physician. 2016;93(5):363-370.
3. Gabriella Bathgate. New diagnosis of hyperthyroidism in primary care. *BMJ*. 2018;362: 2880

5.3.3 HYPOTHYROIDISM

BRIEF DESCRIPTION

- The body requires thyroid hormones for normal metabolism and growth.
- Hypothyroidism is a condition in which there is a reduction in thyroid hormone production.

- In adults, it may be the cause of a slow metabolic rate, systemic problems and dementia.
- The most common reason is decreased production by thyroid glands (called primary hypothyroidism), rarely it could be caused by pituitary abnormalities (secondary)
- Antibody-related thyroid gland destruction, surgical removal of the thyroid, pituitary lesions or surgery, congenital, severe iodine deficiency are the major causes.
- Myxedema coma describes the most severe state of hypothyroidism and is a medical emergency.

CLINICAL FEATURES

- **Symptoms**
    - Patients could remain asymptomatic for several years or they might not recognize the symptoms themselves.
    - Intolerance to cold environments, constipation, weight gain, hair loss, dry skin
    - Hoarse voice, lethargy, memory loss, depressed reflexes, dementia
    - Abnormal menstrual periods and sub-fertility (in adult females)
- **Signs**
    - Puffy face, pallor, slow pulse (usually <60 per minute)
    - Goiter may be present

INVESTIGATIONS

- TSH
- Free T4

DIAGNOSIS

- The diagnosis of hypothyroidism is usually delayed due to lack of recognition.

- A very high index of suspicion should be maintained in any adult woman who presented with fatigue or non-specific symptoms.
- TSH is the best screening test
  - TSH >20 micro unit/ml: highly suggestive primary hypothyroidism
  - Normal TSH: excludes primary hypothyroidism
  - Mildly elevated TSH (<20microunits/ml): needs freeT4 determination
  - Mildly elevated TSH with normal free T4: subclinical hypothyroidism

TREATMENT

OBJECTIVES OF TREATMENT

- Correct level of thyroid hormones gradually
- Improve symptoms
- Prevent complications

NON-PHARMACOLOGIC TREATMENT

- None

PHARMACOLOGIC TREATMENT

- **Levothyroxine**
  - Starting dose
    - Young patients with no cardiovascular disease 100mcg/day
    - Elderly patients with no obvious cardiac disease 50mcg/day
    - Patients with established cardiac disease 25-50mcg/day
  - Dose adjustment
    - Dose adjustment should be made after at least 2-3 months of therapy
    - Dose increments by 25-50mcg/day in 2- 3months
    - Achieving TSH is the target of treatments

  - After normalization of TSH, annual follow up of TSH suffices

FURTHER READING

1. Onyebuchi Okosieme, Jackie Gilbert, Prakash Abraham, Kristien Boelaer et al. Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee. Clinical Endocrinology (2015), 0, 1–10.
2. Birte Nygaard. Primary Hypothyroidism. American Family Physician; March 15, 2015, Volume 91, Number 6.
3. Michelle So, Richard J MacIsaac, Mathis Grossmann. Hypothyroidism: Investigation and management Australian Family Physician; Vol. 41, no. 8, August 2012.

5.4 ADRENAL DISORDERS

5.4.1 ADRENAL INSUFFICIENCY

BRIEF DESCRIPTION

- Adrenal insufficiency is a clinical condition where the amount of cortisol is insufficient to meet the body's needs.
- It results in fluid, electrolyte imbalance and hypoglycemia.
- It may also result in acute circulatory collapse (shock), in a state commonly referred to as adrenal crisis. Adrenal crisis is a medical emergency.
- Adrenal insufficiency could result from pathologies of the adrenal gland itself (called primary) or the pituitary gland (secondary).
- Relative adrenal insufficiency is very common in critical ill patients
- Common causes of adrenal insufficiency
  - ○ Infectious: Tuberculosis, HIV, Meningococcemia
  - ○ Autoimmune destruction of the adrenal gland (Addison's disease)
  - ○ Sudden cessation of corticosteroid therapy after prolonged use

  - Pituitary failure from severe postpartum hemorrhage
  - Pituitary surgery or tumors
  - Stress (e.g., infection, severe trauma, surgery, and dental procedures) are major precipitants of adrenal crisis.

CLINICAL FEATURES

- **Symptoms**
  - Easily fatigued
  - Vague abdominal complaints/abdominal pain
  - Nausea, vomiting, diarrhea, collapse, dehydration, craving for salt
- **Signs**
  - Low blood pressure (postural drop in blood pressure)
  - Darkening of oral mucosa, gums, skin, palms and soles in some patients

DIAGNOSIS

- The diagnosis of adrenal insufficiency is usually delayed and patients suffer from delayed diagnosis
- A high index of clinical suspicion is the most important element in the diagnosis.
- Early morning (8-9AM) serum cortisol <3mcg/dl is strongly indicative and >18mcg/dl excludes the diagnosis.
- Confirmation of adrenal insufficiency needs dynamic testing: refer patients to a hospital where there is endocrine service.

INVESTIGATIONS

- Basal(morning) serum cortisol
- Serum electrolytes: sodium and potassium
- Blood sugar
- CXR, Abdominal ultrasound: to assess the possible cause

- HIV screening
- In adrenal crisis: CBC, ESR, Cultures

TREATMENT

OBJECTIVES OF TREATMENT

- Correct the fluid and electrolyte imbalance
- Replace corticosteroids
- Identify cause and treat any precipitating factor

NON PHARMACOLOGIC TREATMENT

- Encourage fluid and salt intake

PHARMACOLOGIC TREATMENT

- **Acute therapy:** do not wait for confirmation, start treatment based on clinical suspicion
  - **Intravenous fluid replacement**
    - DNS (0.9% Sodium Chloride I with5% dextrose),1000ml, every 4-6 hours
  - **Hydrocortisone**
    - 200 mg stat, followed by 50-100 mg, IV every 6 hours.
    - If there is a plan to take sample for serum cortisol, give dexamethasone 4mg IV every 12hr.
    - Do not rush to change the intravenous hydrocortisone to oral maintenance therapy.
    - Start maintenance oral therapy when the patient is stable enough to be discharged.
- **Adjunct treatment**
  - Treat infection, if present or suspected, with appropriate medication.
- **Maintenance therapy**

- **Glucocorticosteroids:** If available oral hydrocortisone is preferred.
  - Hydrocortisone (tablet), PO, 15 -20mg/day in two to three divided doses.

    OR
  - Prednisolone 5mg, PO, on the morning and 2.5mg in the evening (or 5mg in the morning alone)

    OR
  - Dexamethasone 0.5mg, PO, once in the morning
- **Additional Mineralocorticoid**
  - Fludrocortisone 0.1mg/day. If on hydrocortisone reduce the dose to 0.05mg/day.
- **Sick day glucocorticosteroids dosing**
  - Patients SHOULD NOT STOP treatment if they become ill, rather they should increase the doses.
  - For minor illness such upper respiratory tract infections and fever: Triple the dose for three days (3x 3 rule).
  - For emotional stress double the dose for three days.
  - If there is vomiting: need intravenous hydrocortisone
  - For surgery and labor: give intravenous hydrocortisone preoperatively and until the patient takes oral dose
    - For minor surgery: 25-50mg IV hydrocortisone
    - For major sugary: 100-150mg hydrocortisone/day in two to three divided doses.

REFERRAL

- Ambulatory patients with suspected adrenal insufficiency should be referred for specialist evaluation, diagnosis and management.
- Acutely sick patients who are suspected to have adrenal insufficiency

should be started treatment without any delay.

FURTHER READING

1. Evangelia Charmandari, Nicolas C Nicolaides, George P Chrousos. Adrenal insufficiency. Lancet 2014; 383: 2152–67.
2. Stefan R. Bornstein, Bruno Allolio, Wiebke Arlt, Andreas Barthel et al. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, February 2016, 101(2):364–389.

5.4.2 CUSHING'S SYNDROME

BRIEF DESCRIPTION

- Cushing's syndrome is a clinical syndrome which results from high levels. of cortisol in the blood and is associated with various changes in the body.
- It results in unexplained and rapid weight gain resulting in the development of obesity, hypertension, diabetes and osteoporosis.
- The major causes are pituitary tumor/adenoma, adrenal tumor or prolonged and excessive intake corticosteroids.

CLINICAL FEATURES

- **Symptoms**
  - Symptoms could be subtle as they develop very slowly or asymptomatic
  - Weight gain
  - Change in body habitus and shape: obesity, facial fullness
  - Excessive facial hair
  - Easy fatigability
  - Easy bruising of the skin
  - Menstrual irregularity
  - Labile mood

- **Signs**
  - High blood pressure
  - Truncal obesity
  - Prominent supraclavicular fat pad, rounded or moon'
  - Striae: Wide (>1cm) and purplish or red
  - Hirsutism
  - Proximal muscle weakness

Proximal myopathy, wide purple/red striae, and easy bruising are highly predictive of crushing's syndrome

INVESTIGATIONS

- **Screening biochemical test options**
  1. 1mg overnight dexamethasone suppression test
     - Give 1 mg of dexamethasone at 11 PM to 12 AM (midnight), and measurement of serum cortisol at 8 AM the next morning.
     - A morning cortisol level above 1.8 mcg/dl (50nmol/l) is suggestive of Cushing's syndrome.
  2. 24-hour urine free cortisol: Level 3-4 times the upper limit of normal is highly suggestive
  3. Late evening (11 PM) salivary cortisol
- **Other supportive investigations**
  - Blood sugar, lipid profile
  - Serum electrolytes
- Confirmatory tests should only be ordered and interpret by specialist.
- Imaging should not be ordered without having biochemical confirmation.

DIAGNOSIS

- The diagnosis of Cushing's syndrome starts with high index of clinical suspicion; however, confirmation requires biochemical tests.
- The first step in the diagnosis is to exclude exogenous steroid use (oral, IM, IV)
- Whom to screen with biochemical tests?
  - Those with clinical features highly predictive of Cushing's syndrome
  - Osteoporosis or hypertension in young adults
  - Incidental adrenal mass
- The biochemical testing requires the following three steps;
  1. Confirming high cortisol
  2. Determine if the high cortisol is ACTH-dependent or ACTH-independent
  3. Determine the source of ACTH (if it is ACTH-dependent)
- Patients with suspected Cushing's syndrome should be referred either directly or after doing screening test

TREATMENT

OBJECTIVES OF TREATMENT

- Normalize plasma level of cortisol
- Correct metabolic and electrolyte abnormalities
- Correct blood pressure

NON PHARMACOLOGIC TREATMENT

- Surgery: the main stay of treatment of Cushing's syndrome is surgery (pituitary or adrenal gland surgery depending on the cause)
- The surgery should be done in referral hospitals with experience in doing surgery.

PHARMACOLOGIC

- Manage hypertension and diabetes as per the standard treatment guidelines and refer patient for definitive treatment.

REFERRAL

- All patients suspected to have Cushing syndrome should be referred to a referral hospital with endocrine, neurosurgical and endocrine surgery services.

FURTHER READING

1. Lynnette K. Nieman. Recent Updates on the Diagnosis and Management of Cushing's syndrome. Endocrinol Metab. 2018; 33:139-146.
2. Lynnette K. Nieman, Beverly M. K. Biller, James W. Findling, John Newell-Price et al. The diagnosis of Cushing's syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, May 2008, 93(5):1526–1540.

5.5 MINERAL AND BONE DISORDERS

5.5.1 VITAMIN D DEFICIENCY IN ADULTS

BRIEF DESCRIPTION

- Vitamin D is vital in skeletal health.
- Vitamin D's role in extra skeletal health (cancer, cardiovascular disease, infectious diseases and immune dysregulation) is not clear.
- Overt vitamin D deficiency, characterized by hypocalcemia, hypophosphatemia or osteomalacia is not common in adults but low level of vitamin D with no clinical features associated with it (subclinical deficiency) appears to be very common.
- Adults with prolonged vitamin D deficiency, rarely develop osteomalacia. The optimal serum vitamin D (25(OH) D) level needed for skeletal health is controversial.

- Experts agree a 25(OH) D less than 20ng/mL is likely to be suboptimal for skeletal health.
- Common causes of vitamin D deficiency include decreased intake or absorption, dark skin, reduced sun exposure, drugs which increase vitamin d metabolism (e.g., Phenytoin).

CLINICAL FEATURES

- Asymptomatic: the majority of patients with vitamin D deficiency are asymptomatic
- Symptoms and signs related to osteomalacia: bone pain and tenderness, muscle weakness, and pathological fracture.
- Investigation and diagnosis
- Whom to screen for vitamin D deficiency?
  - The current evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults.
  - It is advisable to screen older individuals, home-bound adults, obese patients, patients with others features of mal
  - Symptomatic individuals should definitely be screened: low serum calcium, hyperphosphatemia, pathological fractures, suspected osteomalacia or osteoporosis.
- Cut-off point for defining deficiency
  - < 20ng/ml………deficiency
  - 20-30 ng/ml……..insufficient for skeletal health
  - >30ng/ml…...... …sufficient for skeletal health
- Other investigations
  - Serum calcium, phosphorus, PTH, alkaline phosphatase level are important in patients who are symptomatic

TREATMENT

OBJECTIVES OF TREATMENT

- Prevent fractures in vulnerable individuals
- Prevent and correct skeletal symptoms

NON-PHARMACOLOGIC TREATMENT

- Dietary advice
- Adequate sun exposure for institutionalized or home-bound elderly
- Exercise

PHARMACOLOGIC TREATMENT

- **Vitamin D levels <20ng/ml**
  - Vitamin D3 or D2, 50,000 IU once per week for 8 weeks
  - Followed by maintenance therapy 800IU daily
  - Additional calcium 1000mg/day
  - Follow up 25(OH) D level: after three to four months of maintenance therapy
- **Vitamin D levels 20 - 30ng/ml**
  - Vitamin D3 or D2 800 IU/daily
  - Additional calcium 800-100omg/day
  - Follow up 25(OH) D level: after three to four months of maintenance therapy
- **Vitamin D levels >30ng/ml**
  - No active treatment
  - In older individuals with a level between 20-30ng/ml vitamin D3 or D2 600-800mg/day can be given.

FURTHER READING

1. Stefan Pilz, Armin Zittermann, Christian Trummer, Verena Theiler-Schwetz et al. Vitamin D testing and treatment: a narrative review of current evidence. Endocrine Connections (2019) 8, R27–R43.
2. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, July 2011, 96(7):1911–30

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5.5.2 OSTEOPOROSIS

BRIEF DESCRIPTION

- Osteoporosis literally means porous bone.
- It is a skeletal disorder characterized by low bone mass and bone architecture deterioration leading to bone fragility and increased risk of fracture.
- The three major types of osteoporosis;
    1. Postmenopausal (type I)
    2. Involutional (type II): in both old men and women older due to subtle increase in both resorption
    3. Secondary (type III)**:** due to other diseases or drugs
- The major risk factors for osteoporosis are older age, early menopause, excessive alcohol use, excessive caffeine intake, tobacco use, low physical activity level, low body weight, low vitamin D or calcium intake, history of falls or fractures, family history of osteoporotic fractures.
- Major causes of secondary osteoporosis
    - o Cancer: Multiple myeloma, bone metastases
    - o Inactivity or immobilization

- Chronic kidney disease
- Endocrine disorders: Cushing's syndrome, hyperthyroidism
- Chronic inflammatory diseases: Rheumatoid arthritis, SLE, IBD
- Medication: long term use of steroids, anticonvulsants, loop diuretics, PPI
- Malnutrition

CLINICAL FEATURES

- **Symptoms**
    - Patients with osteoporosis are asymptomatic until they develop fracture
    - Symptoms related to fracture
        - Pain
        - Impaired mobility
        - Respiratory difficulty
        - Deformity
- **Signs**
    - The signs are related to the presence of fractures
        - Loss of height
        - Kyphosis
        - Chest deformity,
        - Rib-pelvis overlap
        - Protuberant abdomen

INVESTIGATIONS

- BMD measurement: DEXA scan
- X-ray of the spine

  - It is not diagnostic but can help in the diagnostic process
  - X-ray related changes occur very late
  - Increased lucency, cortical thinning, increased density of end plate, anterior wedging and biconcavity of vertebrae are the major signs
- Vitamin D (25(OH)D, calcium, phosphorus and PTH level

DIAGNOSIS

- The diagnosis of osteoporosis can be made based on clinical or bone mineral density measurement
  - **Clinical osteoporosis diagnosis**
    - One or more fragility (low trauma fracture) of the spine, hip, femoral neck, wrist that happens in high-risk individuals.
  - **Bone mineral density (BMD) based diagnosis:** Dual energy x-ray absorptiometry (DEXA) scan is used to measure bone density.
    - T and Z scores are used to report DEXA scan findings.
    - The T-score is a comparison of a person's bone density with that of a healthy 30-year-old of the same sex.
    - The Z-score is a comparison of a person's bone density with that of an average person of the same age and sex
      - **Diagnosis of Osteoporosis (lumbar Spinal or hip, 1/3 radial):** T-score ≤ –2.5
      - **Diagnosis of severe/established osteoporosis**: ≤ –2.5 + one or more fragility fractures

TREATMENT

OBJECTIVES OF TREATMENT

- Prevent fragility fracture
- Decrease/prevent disability

NON-PHARMACOLOGIC TREATMENT

- Prevention of falls
- Muscle strength and balance exercises
- Diet: adequate calorie, calcium and Vitamin D intake
- Decrease alcohol intake
- Decrease caffeine intake
- Quit smoking
- Sun exposure

PHARMACOLOGIC TREATMENT

- **First line**: **Bisphosphonates**
    - Indications to start bisphosphonates
        - The presence one or more fragility fracture (commonly hip or spine)
        - DEXA scan diagnosis T-score ≤ –2.5
        - Long term corticosteroid steroid use: prophylactic
    - Check serum vitamin D and calcium level. Correct deficiencies before starting bisphosphonates.
    - Specific bisphosphonate doses for treatment of osteoporosis

Table 5.10: bisphosphonate doses for treatment of osteoporosis

Drug	Therapeutic dose
Alendronate	70mg PO per week
Ibandronate	150mg PO per month
Zolendronic acid	5mg IV per year

Table 5.11: Specific bisphosphonate doses for prevention of osteoporosis in long-term corticosteroid users.

	Prophylactic dose
Alendronate	35mg PO per week
Ibandronate	150mg PO per month
Zoledronic acid	5mg IV every two years

- ○ Duration of therapy for osteoporosis: After 5-10 years of oral bisphosphonates or 3-6 years of IV bisphosphonates, a 3- 5-year discontinuation (holidays) should be given if there is no fracture in between.
- ○ Contraindications: esophageal disorder, advanced CKD (eGFR <30ml/min)
- ○ Common adverse effects: Esophageal ulcerations, perforations, bleeding, sever muscular/bone /joint pains
- ○ Administration of oral bisphosphonates
  - – In empty stomach (in the morning after an overnight fasting)
  - – With a full glass of water
  - – Wait for at least 30 minutes before taking food, other beverages (other than water) or other medications.
  - – Stay upright for at least 30 minutes before reclining (sleeping),
    - ▪ IV Zoledronic acid: For patients who do not tolerate or can't adhere to the dosing precautions of oral bisphosphonates.
  - – Zoledronic acid administration:
    - ▪ Give paracetamol 1000mg, 30 minutes before administration.
    - ▪ Reconstitute powder with 5 ml of sterile water for injection

    - Once the powder is fully dissolved, dilute further in 100 ml NS or D5W.
    - Give the infusion over at least 15 minutes.

- **Additional pharmacologic therapy**
  - Vitamin D: 800IU/day

FURTHER READING

1. American association of clinical endocrinologists/American college of endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis— 2020 update. ENDOCRINE PRACTICE Vol 26 (Suppl 1) May 2020. http://www.endocrinepractice.org. DOI: 10.4158/GL-2020-0524
2. Treatment of Low BMD and Osteoporosis to Prevent Fractures: Updated Guideline from the ACP. Ann Intern Med. June 6, 2017;166(11):818-839.

CHAPTER 6:

GASTROINTESTINAL TRACT AND HEPATOBILIARY DISEASES

6.1 DYSPEPSIA AND PEPTIC ULCER DISEASE

BRIEF DESCRIPTION

- Dyspepsia describes a wide and common clinical entity which presents in one of the three ways:
    1. Epigastric pain/burning (epigastric pain syndrome)
    2. Postprandial fullness
    3. Early satiety
- Dyspepsia is caused by a number of disorders.
- The most common cause is functional (non-ulcer) dyspepsia followed by peptic ulcer disease.
- Gastro esophageal reflux disease (GERD), gastric cancer, medication induced dyspepsia, biliary pain, chronic abdominal wall pain and pancreatitis are other possible causes.

CLINICAL FEATURES

- Depending on the type of dyspeptic syndrome patients may present with predominant epigastric burning sensation/pain/discomfort, postprandial discomfort and fullness or be unable to finish a regular meal.

ALARM SIGNS (need to be further investigation for cancer)

- Advanced age (>55years)
- Previous gastric surgery
- Unintended weight loss
- Persistent vomiting
- Hematemesis
- Progressive dysphagia/Odynophagia
- Otherwise, unexplained anemia
- Palpable abdominal mass
- Lymphadenopathy
- Jaundice

INVESTIGATIONS

- **H. Pylori test**: IgG serology or stool antigen or 13C-urea test
- Hemoglobin/hematocrit, stool for occult blood-when indicated
- Upper GI endoscopy

- H. Pylori test needs to be done for the following patients
  - Long standing dyspepsia
  - Younger than 55 years
  - No alarm symptoms
  - No use of non-steroidal anti-inflammatory drugs
  - No features of GERD (Gastro Esophageal Reflux Disease)
- "Test and treat" for H. Pylori can be practiced in these group of individuals

TREATMENT

OBJECTIVES OF TREATMENT

- Decrease symptoms/improve quality of life
- Prevent development of complications

NON PHARMACOLOGIC

- Avoid offending foods/drinks

PHARMACOLOGIC

- **H. Pylori negative**
  - First line: **Proton pump inhibitors**
    - Omeprazole, 20mg P.O., twice per day for 4-8 weeks
    - Esomeprazole, 40mg P.O., daily for 4-8 weeks
    - Pantoprazole, 40mg P.O., BID for 4-8 weeks
  - Alternatives:**H2 receptor blockers**
    - Cimetidine, 400mg P.O., BID for 4-8 weeks
    - Ranitidine, 150mg P.O. BID for 4-8 weeks
    - Famotidine, 20-40mg P.O. daily for 4-8 weeks
- **H. Pylori positive: H. pylori eradication therapy**
  - **First line therapy**: All drugs for 7-14 days
    - Amoxicillin, 1gm, P.O. BID

      PLUS
    - Clarithromycin, 500mg, P. O., BID

      PLUS
    - Proton pump inhibitors (see the daily doses above)
  - **Alternative** (for penicillin allergic patients): This regimen has a higher failure rate. All drugs should be given for 7-14 days

    - Clarithromycin, 500mg P.O. BID

      PLUS

    - Metronidazole, 500mg, P.O. BID

      PLUS

    - Proton pump inhibitors (see the daily doses above)

6.2 GASTROESOPHAGEAL REFLUX DISEASE (GERD)

BRIEF DESCRIPTION

- Gastroesophageal reflux refers to the return of stomach contents in to the esophagus.
- Some degree of brief reflux occurs physiologically; usually after a meal or during sleep.
- GERD refers to a pathologic reflux associated with symptoms and complications.
- GERD is a common in primary care practice. Due to its symptoms, it can also be misdiagnosed.
- Based on the endoscopic appearance GERD is classified in to two types: Erosive and non-erosive.
- Erosive GERD (Erosive esophagitis) is diagnosed when there are endoscopically visible breaks in the esophageal mucosa while non-erosive GERD shows no visible mucosal injury on endoscopy.
- GERD is associated with significant esophageal or extraesophageal complications.
  - **Esophageal complications**
    - Barrett's esophagus: a precancerous change in the esophageal mucosa (from squamous epithelium to columnar epithelium)
    - Esophageal stricture: which manifests with solid food dysphagia

and intermittent food impaction?

- **Extraesophageal complications**
    - Triggering Asthma
    - Laryngeal and pharyngeal reflux: which manifests with chronic cough, repetitive throat cleaning, hoarseness of voice

CLINICAL MANIFESTATIONS

- **Symptoms**
- The two major symptoms of GERD which are considered classic (typical) are heartburn and regurgitation.
    - Heartburn is a commonly described by patients as a burning sensation behind the sternum (retrosternal area).
    - Regurgitation is defined as back flow of gastric contests in to the mouth or pharynx. Patients feel an acidic (sour) content coming to the mouth mixed with small amounts of undigested food.
- **Other symptoms**
    - Chest pain: GERD associated chest pain can mimic angina (pain from ischemic heart disease)
    - Triggering asthma attacks (wheezing)
    - Hoarsens of voice
    - Persistent cough
    - Nausea
    - Sensation of a lump in the throat (Globus sensation)
    - Increased salivation (Water brash)

DIAGNOSIS

- In patients with typical symptoms i.e., heartburn or regurgitation, the diagnosis of GERD can be considered on clinical grounds without additional investigations, if there are no alarm signs. In such cases empiric therapy should be started.

INVESTIGATIONS

- **Upper GI (gastrointestinal) endoscopy**
  - Endoscopy is not necessary to make a diagnosis of GERD but it is indicated in patients with alarm features to see evaluate for possible malignancy.
  - The alarm features are weight loss, age above 60 years, iron deficiency anemia, dysphagia, persistent vomiting or family history of cancer in parents or siblings.
  - If GERD symptoms have been there for more than 5-10 years, endoscopy can be considered to look for evidence of Barrett's esophagus.

TREATMENT

OBJECTIVES OF TREATMENT

- Relive symptoms
- Decrease the risk of complications such as Barrett's esophagus, esophageal stricture

NON-PHARMACOLOGIC TREATMENT

- **Life style modifications**
  - Weight loss in overweight and obsess patients.
  - Avoiding meals 2 -3 hours before bed is also advisable.
  - Head elevations to 15-20 cm during sleep.
  - Dietary selection should not be forced or recommended universally unless patients identify the specific food item as triggering factor. e.g., caffeine, spicy foods, food with high fat content, carbonated beverages, and chocolate)
  - Other life style modifications are not supported by evidence.
- **Surgery**

  - Surgical intervention (usually fundoplication) in GERD patients is rarely indicated. Surgery ma may be considered in the following circumstances:
    - Large hiatal hernia causing the reflux symptoms
    - Evidence of aspiration
    - Esophagitis refractory to medical therapy
    - Persistent symptoms documented as being caused by refractory GERD: after checking compliance to PPI and optimizing PPI use.

PHARMACOLOGIC TREATMENT

- **First line: Proton-pump inhibitors (PPIs)**
  - No major difference in between the available PPIs
    - Omeprazole 40mg PO daily for 8 -12 weeks

      OR
    - Esomeprazole 40mg PO daily for 8-12 weeks

      OR
    - Pantoprazole 40mg PO daily for 8-12 weeks
- Stop therapy on symptom resolution to assess response
- After the first 8 -12 weeks, resume therapy as needed
  - Intermittent

    OR
  - On demand
- **Alternatives:** If PPIs are not available and the symptoms are mild Histamine-2 receptor blockers (H2 blockers) can be considered as alternatives.
    - Cimetidine 400mg BID for 8 weeks

      OR

  - Ranitidine 150mg BID for 8 weeks

    OR

  - Famotidine 20mg BID for 8 weeks

REFERRAL

- Patients with alarm symptoms need to be referred without any delay after the initial evaluation.
- Patients with persistent symptoms after 8 weeks of therapy should be referred for specialist evaluation and follow up.

FURTHER READING

1. Philip O. Katz   Lauren B. Gerson, and Marcelo F. Vela. Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am J Gastroenterol 2013; 108:308 – 328
2. World Gastroenterology Organization Global Guidelines: GERD, Global Perspective on Gastroesophageal Reflux Disease. Update October 2015.

6.3 GASTROINTESTINAL BLEEDING

6.3.1 UPPER GASTROINTESTINAL (GI) BLEEDING

BRIEF DESCRIPTION

- Upper GI bleeding refers to gastrointestinal blood loss originating from the gastrointestinal tract is proximal to the ligament of Treitz at the duodenojejunal junction.
- It can be overt or occult bleeding.
- Overt upper GI bleeding can manifest in the following ways:
  - Hematemesis: vomiting of frank red blood or a “coffee-grounds” material.

  - Melena: Passage of black, tarry stool
  - Hematochezia: passage of bright red or maroon (dark red) blood from the rectum. Upper GI bleeding causes hematochezia rarely, when it is massive and very acute.
- Occult upper GI bleeding present with symptoms anemia such as lightheadedness, or a positive fecal occult blood test on routine testing.
- The causes of upper GI bleeding are summarized in the table below.
- The two major causes that should be considered in every patient with overt upper GI bleeding are peptic ulcer disease and esophageal varices.

Table 6.1: Causes of Upper GI bleeding

1. Peptic ulcer disease
2. Esophageal varices
3. Gastroduodenal erosions
4. Mallory-Weiss tears (esophageal mucosal tear due to vomiting or retching)
5. Esophagitis
6. Vascular malformations,
7. Neoplasm
8. Coagulopathy
9. Obscure upper GI bleeding: often from small intestinal lesions

CLINICAL FEATURES

- **Symptoms**
  - Nausea
  - Vomiting of bright red blood or coffee-ground matter
  - Melena

- **Hematochezia**: rare in upper GI bleeding but can occur in massive acute bleeding.
- Symptoms related to the underlying cause;
  - Medication history: antiplatelet (aspirin, clopidogrel), non-steroidal anti-inflammatory drugs or anticoagulants
  - Symptoms of portal hypertension or liver cirrhosis in patients with variceal bleeding e.g., ascites, fatigue.
  - The bleeding in varices is generally bright red, painless, brisk, and voluminous.
  - Long standing epigastric pain: Suggestive of peptic ulcer disease
  - Preceding forceful vomiting or retching suggests Mallory-Weiss tears
  - **Weight loss**: may indicate neoplasm

- **Signs**
- In general, the physical signs (physical examination focuses on the following two elements)

1. **The hemodynamic status of the patient and the degree of anemia**
   - Blood pressure: check for supine BP. If supine BP is normal check for postural hypotension (supine, followed by measurement after 3 minutes of standing
   - Pulse rate: assess for resting tachycardia
   - Degree of pallor
2. **Signs of the underlying cause of the upper GI bleeding**
   - Signs of chronic liver disease or portal hypertension indicating the possibility of bleeding varices: Ascites, splenomegaly, encephalopathy.
   - Other site bleeding: platelet related disorders or coagulopathies

INVESTIGATIONS

- CBC (complete blood count)
- Serial hemoglobin/hematocrit every 8 hour: the initial hemoglobin/ hematocrit may be normal as the loss is whole blood (both plasma and cells)
- Coagulation profile: PT (INR) and PPTT
- Urea and Creatinine
- Liver enzymes
- Upper GI endoscopy; see above on diagnosis

DIAGNOSIS

- The diagnosis of upper GI bleeding is made on clinical grounds mainly based on history: a history of hematemesis or melena establishes the diagnosis.
- The next step in the diagnosis is trying to establish the cause of the upper GI bleeding.
- In addition to history and physical examination, identifying the cause of the upper GI bleeding requires upper GI endoscopy.
- Upper GI endoscopy has both diagnostic and therapeutic value.

RISK STRATIFICATION

- There are a few risk stratifications tools which are useful to assess the likelihood of a person with upper GI bleeding to need further interventions like endoscopic treatment and transfusion.
- The Glasgow-Blatchford bleeding score (GBS) is one of the scores. It is simple risk stratification tool which does not require endoscopy. We recommend using the score.

Table. 6.2: Glasgow-Blatchford bleeding score (GBS)

Risk marker	Value	Score
• Urea (blood urea) (mg/dl)	38 - 46	2
	47 - 57	3
	58 - 146	4
	≥147	6
• Hemoglobin (g/dl) in males	12 - 13	1
	10 - 12	3
	< 10	6
• Hemoglobin (g/dl) in females	10 - 12	1
	< 10	6
• Systolic BP (mmHg)	100 - 109	1
	99 - 90	2
	< 90	3
• Pulse ≥100 (per min)		1
• Presentation with melena		1
• Presentation with syncope		2
• Hepatic disease		2
• Heart failure		2
Note: Score 0: low risk Score > 0: high risk, keep in hospital as the patient is likely to require transfusion or endoscopic intervention Score > or = 8: requires ICU admission		

TREATMENT

OBJECTIVES OF TREATMENT

- Hemodynamic restoration
- Arresting or decreasing bleeding
- Preventing recurrence of bleeding

PHARMACOLOGIC AND NON-PHARMACOLOGIC TREATMENT

- **Hemodynamic stabilization**
  - Monitor airway, blood pressure and heart rate.
  - Do NOT give patient anything by mouth
  - Establish two large bore IV lines (16 gauge)
  - Treat hypotension initially with rapid, bolus infusions of isotonic crystalloid
  - Provide transfusion if either of the following is present
    - Hemodynamic instability (hypotension) is present.
    - Hemoglobin <9 g/dL in high-risk patients (e.g., elderly, coronary artery disease)
    - Hemoglobin <7 g/dL (70 g/L) in low-risk patients
- **Pharmacotherapy for all patients**
  - **Intravenous proton pump inhibitor**
    - Omeprazole 80mg IV loading followed by 40mg IV BID

      OR
    - Esomeprazole 40 mg IV BID

      OR
    - Pantoprazole 40 mg IV BID

- **Arresting bleeding**
- **Endoscopic** therapy is the main stay of therapy to arrest bleeding.
    - After hemodynamic stabilization consult or refer to facility with endoscopic services.
    - Balloon tamponade may be performed as a temporizing measure for patients with uncontrollable hemorrhage after tracheal intubation.
- **Open surgery**
- **Indica**tions for surgery;
    - Hemodynamic instability despite vigorous resuscitation (> 3 units three of transfusion)
    - Shock associated with recurrent hemorrhage
    - Perforated PUD along with bleeding
    - Failed endoscopic therapy for bleeding PUD
- No access to endoscopy therapy with ongoing bleeding
- Relative indications: difficult crossmatch, refusal of transfusion, shock on presentation,

- **Treating the underlying cause**
    - Patients with H. Pylori associated ulcer bleeding should receive eradication therapy.
    - In NSAID or Aspirin associated bleeding ulcers: stop the drug and re-evaluate the need.
    - Anticoagulants: stop and re-evaluate for continued need, dose adjustment if c
    - Variceal bleeding: band ligation and non-selective beta-blocker therapy (propranolol)

- o Idiopathic (non-H. pylori, non-NSAID) ulcers: long-term PPI is recommended

REFERRAL

- All patients with upper GI bleeding should be referred to hospital with endoscopic therapy facilities after hemodynamic stabilization and starting intravenous PPI.

FURTHER READING

1. Adrian J Stanley, Loren Laine. Management of acute upper gastrointestinal bleeding. BMJ 2019;364: l536.
2. Amrit K. Kamboj, Patrick Hoversten, and Cadman L. Leggett. Upper Gastrointestinal Bleeding: Etiologies and Management. Mayo Clin Proc. 2019;94(4):697-703.
3. Management of Nonvariceal Upper Gastrointestinal Bleeding: Guideline Recommendations from the International Consensus Group. Ann Intern Med. 2019; 171:805-822.
4. Karstensen John Gásdal et al. Nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Cascade Guideline. Endoscopy International Open 2018; 06: E1256–E1263.

6.3.2 LOWER GASTROINTESTINAL (GI) BLEEDING

BRIEF DESCRIPTION

- Gastrointestinal (GI) Bleeding refers to any bleeding that occurs from the mouth to the anus. Anatomically GI bleeding is divided in to upper and lower.
- The ligament of Treitz is used as the anatomic reference to differentiate lower and upper GI bleeding.
- The incidence of lower GI bleeding is higher in older age groups, particularly in those taking anti-platelet agents like aspirin, non-steroidal

anti-inflammatory drugs or anticoagulants.

- Lower GI bleeding can be overt or occult.
  - Overt lower GI bleeding presents with either frank red bleeding (hematochezia) or dark, tarry stool (melena).
  - Occult GI bleeding presents with evidence of iron deficiency anemia but no hematochezia or melena.
- Over GI bleeding is labeled to be massive when it is associated with hemodynamic instability.
- The major causes of lower GI bleeding are categorized as follows:
  - Vascular causes
  - Hemorrhoids
  - Ischemic bowel
  - Vascular dysplasia (angiodysplasia)
  - Post procedure (post polypectomy)
    - **Neoplastic causes**
  - Colon cancer
  - Polyps
    - **Anatomic causes**
  - Diverticulosis
    - **Inflammatory causes**
  - Inflammatory bowel disease
  - Infectious colitis

CLINICAL MANIFESTATIONS

- **Symptoms**
    - **Hematochezia:** pass**age of bright red or** dark red (maroon)

blood or clots per rectum.

- Bleeding from the left colon tends to be bright red in color while bleeding from the right colon appears to be dark or maroon colored and may be mixed with stool.
- Bleeding from the right colon might rarely cause melena (the stool itself is dark)
    - **Symptoms of anemia or hemodynamic compromise**: fatigue, postural dizziness, light headedness

- **Signs**
    - **Signs of hemodynamic compromise**:
- Hypotension (supine or postural)
- Resting tachycardia.
    - **Signs of anemia**
- Pallor
- Tachycardia
- Ejection systolic murmur

INVESTIGATIONS

- The following important investigation in patients with lower GI bleeding
    - CBC (complete blood count): in massive acute bleeding the hemoglobin may appear normal.
    - Serial hemoglobin; every 8 hours
    - Coagulation studies: INR (PT) and PTT
    - Liver enzymes
    - BUN and creatinine
- **Colonoscopy**: **when the clinical diagnosis is lower GI bleeding**

- **Upper GI endoscopy: when the clinical diagnosis is upper GI** bleeding.

DIAGNOSIS

- The diagnosis of lower GI bleeding requires the following important steps:
  1. **Identifying whether the bleeding is upper or lower GI in origin.**
     - Massive upper GI bleeding can cause hematochezia; hence, differentiating Upper from lower GI bleeding is necessary.
     - The presence of hemodynamic instability favors upper GI bleeding
     - The presence of clots suggests lower GI bleeding
     - When there is suspicion of upper GI source: insert NG tube and do gastric lavage with normal saline
       - Gastric lavage with coffee-ground material or bright red blood= upper GI bleeding
       - Gastric lavage is bilious = lower GI bleeding
       - If the gastric lavage is neither of the above = indeterminate (it can be either of the two)
  2. **Identifying possible causes or precipitants of the bleeding.**
     - The history should focus on the following
       - **Medicat**ions: Antiplatelets (e.g., Aspirin or clopidogrel), non-steroidal anti-inflammatory drugs (e.g., Diclofenac, indomethacin, ibuprofen), anticoagulants
       - Prior history of bleeding
       - Significant abdominal pain: suggests inflammatory or ischemic bowel disease or perforation
       - Significant **weight loss**: suggests malignancy
     - Digital rectal examination

3. **Localization of the bleeding and definitive diagnosis**
    - All patients with a clinical diagnosis of lower GI bleeding require colonoscopic examination to identify the cause of bleeding, arrest the bleeding if identifiable.

TREATMENT

OBJECTIVES OF TREATMENT

- Restore hemodynamic status
- Correct precipitating factors

INITIAL TREATMENT AND REFERRAL

- The following are components of the initial treatment of patients suspected of acute lower GI bleeding;
- Hemody**namic status evaluation and resuscitation**
    - In patients with hemodynamic compromise secure two wide bore IV cannuale and resuscitate with crystalloids.
    - While crystalloids are being given, blood should be requested for transfusion.
    - Do not depend on the initial hemoglobin or hematocrit to for transfusion, as it is apparently ("falsely") normal.
- **Discon**tinue antiplatelets, non-steroidal anti-inflammatory drugs or anticoagulants
- Correc**t coagulopathies**
    - E.g., If INR is high or patients are on warfarin, give fresh frozen plasma and/or vitamin K

REFERRAL

- Patients should be referred to a facility with gastroenterology specialty service for colonoscopy, after hemodynamic stabilization.
- In patients who continue to bleed massively and who are unstable to be transferred to a center with colonoscopy facility, surgical consultation

should be made.

FURTHER READING

1. Lisa L. Strate and Ian M. Gralnek. ACG Clinical Guideline: Management of Patients with Acute Lower Gastrointestinal Bleeding. Am J Gastroenterol 2016; 111:459–474
2. Tomonori Aoki, Yoshihiro Hirata, Atsuo Yamada, Kazuhiko Koike. Initial management for acute lower gastrointestinal bleeding. World J Gastroenterol 2019 January 7; 25(1): 69-84
3. Oakland K, et al. Diagnosis and management of acute lower gastrointestinal bleeding: guidelines from the British Society of Gastroenterology Gut 2019;68:776–789

6.4 NAUSEA AND VOMITING

BRIEF DESCRIPTION

Table 6.3: Definitions of terms (adapted from American Gastroenterological Association)

Term	Definition
Nausea	The unpleasant sensation of the imminent need to vomit; it may or may not lead to vomiting.
Vomiting	Forceful oral expulsion of gastric contents associated with contraction of the abdominal and chest wall musculature.
Regurgitation	return of food into the mouth without force. It should be differentiated from vomiting which is characterized by forceful expulsion of food using abdominal and diaphragmatic muscles.
Retching	Spasmodic respiratory movements against a closed glottis with contractions of the abdominal musculature without expulsion of any gastric contents.
Sitophobia	Fear of eating because of subsequent or associated discomfort

Nausea and vomiting are common problems in clinical practice. The presentation can be acute or chronic (persistent) or cyclic.

- Vomiting is physiologic response which is intended to protect a person from harmful ingested substances.
- Pathological nausea and vomiting are symptoms of an underlying disease or medications.
- The etiologies of nausea and vomiting are varied. The table below summarizes the common causes of nausea and vomiting.

Table 6.4: Common causes of nausea and vomiting

Etiologic category	Common etiologies
• **Medications/ toxins**	• Almost all medications can cause nausea and vomiting. • The following are typical examples ○ Chemotherapeutic agents ○ Cardiovascular drugs: digoxin, antiarrhythmics, beta-blockers ○ Analgesics: Tramadol, non-steroidal anti-inflammatory drugs ○ Antibiotics and antivirals ○ Oral contraceptive pills ○ Anticonvulsants ○ Theophylline ○ Alcohol

- **Gastrointestinal disorders**	- Mechanical **obstruction** o Gastric outlet obstruction o Small bowel obstruction - **GI and intraperitoneal pathologies** o Peptic ulcer disease o Appendicitis o Cholecystitis o Pancreatitis o Hepatitis o Mesenteric ischemia o Intra-abdominal malignancies - **Functional disorders** o Non-ulcer dyspepsia o Diabetic gastroparesis o Organic gastrointestinal disorders
- **Infectious causes**	- **Gastrointestinal infections** o Viral gastroenteritis o Bacterial gastroenteritis - **Non-gastrointestinal infections** o Otitis media o Acute febrile illnesses: Malaria, typhoid fever
- **Endocrinologic and metabolic causes**	- **Endocrine cause** o Pregnancy o Diabetic ketoacidosis o Addison's disease - **Metabolic causes** o Uremia o Acute intermittent porphyria

• **CNS and psychiatric causes**	• **Migraine** • **Increased intracranial pressure** ○ Malignancy ○ Intra cranial hemorrhage ○ Brain abscess ○ Meningitis ○ Hydrocephalus ○ Pseudotumor cerebri • **Psychiatric disease** ○ Psychogenic vomiting ○ Anxiety disorders ○ Depression ○ Anorexia nervosa ○ Bulimia nervosa • **Labyrinthine disorders** ○ Motion sickness ○ Labyrinthitis ○ Tumors ○ Meniere's disease
• **Postoperative nausea and vomiting**	
• **Cyclic vomiting syndrome**	
• **Miscellaneous causes**	○ Starvation ○ Myocardial infarction ○ Congestive heart failure

APPROACH TO A PATIENT WITH NAUSEA AND VOMITING

- In most circumstances the causes of nausea and vomiting are obvious from the history and physical examination.
- The following clinical questions need to be answered with the history and physical examination.
    - Does the patient have hemodynamic compromise or dehydration?
    - Is the presentation indicative of an abdominal emergency such as intestinal obstruction, gastric perforation, appendicitis, pancreatitis, acute cholecystitis or peritonitis?
    - Has the patient taken a medication or a toxin (e.g., alcohol) potential that can cause the vomiting?
    - Does the patient have other symptoms and signs which indicate the possible etiology of nausea and vomiting?
- **Clinical clues to potential causes**
    - Early morning vomiting: pregnancy, increased intracranial pressure
    - Vomiting during eating: psychiatric causes
    - Severe abdominal pain: acute abdominal emergencies
    - History of diabetes or polyuria: DKA
    - Abdominal distension, failure to pass feces or flatus: bowel obstruction
    - Feculent vomiting: intestinal obstruction
    - Vomiting of food eaten several hours before: gastric obstruction or gastroparesis.
    - Heartburn: gastroesophageal reflux disease (GERD)
    - Vertigo and nystagmus: vestibular disorders
    - Headache: migraine or raised intracranial pressure.
    - Focal neurologic deficit: Increase intracranial pressure

  - Diarrhea, malaise: infectious
  - Significant, progressive weight loss: malignancies
- Investigation should be directed based on the suspected diagnosis after history and physical examination.
  - Real function test and electrolytes
  - Plain abdominal X-ray: when intestinal obstruction is suspected
  - Abdominal ultrasound: when acute cholecystitis, appendicitis and other intra-abdominal pathologies are suspected.
  - Endoscopy: for patients with chronic nausea and vomiting, if the cause is not obvious.

TREATMENT

GENERAL PRINCIPLES OF TREATMENT

- The following are the major principles in the treatment of a patient with nausea and vomiting.
  1. **Evaluating for emergency conditions**: intestinal obstruction, bowel perforation, peritonitis, DKA.
  2. **Correction of fluid and electrolyte abnormalities**
  3. **Treatment of the underlying cause:** Examples
     - Surgery for obstruction, perforation, appendicitis etc.
     - Management of diabetic ketoacidosis.
     - Treatment of raised intracranial pressure
  4. **Symptomatic treatment of nausea and vomiting**
- Correction of fluid and electrolyte abnormalities
  - In patients with persistent vomiting, signs of dehydration or hypotension give intravenous crystalloids.
  - The preferred fluid in normal saline (NS) for the initial resuscitation, followed by NS with addition of 20 - 40mmol of potassium per liter of fluid.

- **Symptomatic treatment**
  - Symptomatic treatment should not prevent looking for the possible causes.
  - Non pharmacologic symptomatic treatments
    - Take small meals frequently
    - Reduce the fat content of meals
    - Avoid carbonated beverages.
    - Use more liquid diet than solid until symptoms subside
  - Pharmacologic symptomatic treatment; see the table below

Table 6.5: Pharmacologic treatment and preventive option for nausea and vomiting

Drugs	**Major indications**	**Adult dose**	**Common adverse effects**
• **Antihistamines**			
Dimenhydrinate	Motion sickness Vertigo	50 to 100mg, PO/IM, every 6 to 8 hours. Maximum 400mg/day	Drowsiness, blurred vision, palpitation
Diphenhydramine	>>	25 to 50 mg, PO/IV/IM, every 6 to 8 hours. Maximum 400mg/day	Drowsiness, blurred vision, palpitation
• **Prokinetics-Dopamine(D2) receptor antagonist**			
Metoclopramide	Gastroparesis Postoperative Chemotherapy Hiccups	10 mg PO, IM, IV every 6 – 8 hours. Maximum 40mg/day	Extrapyramidal side effects (dystonia, akathisia, dyskinesia,)

Domperidone	Gastroparesis	10mg PO every 8 hours Maximum= 30mg	Headache and dry mouth
• **Phenothiazines**			
Chlorpromazine	Motion sickness Vertigo Postoperative Severe nausea and vomiting,	25 to 50 mg, PO/IM/IV every 6 to 8 hours	Sedation, hypotension, extrapyramidal side effects.
Promethazine	>>	2.5 to 25 mg every 4 to 6 hours as needed	>>
• **Serotonin receptor antagonists—5-HT3**			
Ondansetron	Chemotherapy Postoperative Severe nausea and vomiting	8mg PO/IV every 12 hour	Headache, constipation, dizziness
• **Corticosteroids**			
Dexamethasone	Adjunct for chemotherapy induced nausea and vomiting	4 to 8mg 30 minutes before chemotherapy	Insomnia, mood changes

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6.5 CHRONIC DIARRHEA IN ADULTS

BRIEF DESCRIPTION

- Diarrhea is one of the most common symptoms for which patients seek medical attention.
- **Diarrhea** is defined as an increased number (three or more) or decreased consistency of stools (soft or liquid) from a person's baseline during a 24-hour period.
- Chronic diarrhea is defined as diarrhea which stays for more than four weeks.
- Chronic diarrhea has several etiologies and a thorough clinical evaluation is needed to reach to the etiology.
- In any adult presenting with chronic diarrhea HIV testing is needed; as the causes and the approach to chronic diarrhea in patients with HIV are different from those with no HIV.
- Chronic diarrhea IS categorized in to three:
    1. Watery
    2. Fatty (malabsorptive)
    3. Inflammatory (High pus cell count or frank pus, occult blood or frank blood)

Table 6.6: Common causes of chronic diarrhea in adults

Watery	Fatty(malabsorptive)	Inflammatory
1. **Secretory:** large volumes, nocturnal, unrelated to food intake) • Bacterial toxins • Chronic giardiasis • Alcoholism • Medications • Celiac disease • Microscopic colitis • Ischemic bowel • Hyperthyroidism (increased motility). • Postsurgical (e.g. Post intestinal resection)	**1. Malabsorption** (damage to or loss of absorptive surface) • Celiac sprue (gluten enteropathy • Tropical sprue • Whipple disease • Gastric bypass • Short bowel syndrome • Bacterial overgrowth syndrome	1. **Inflammatory bowel disease** • Crohn disease • Ulcerative colitis

2. **Osmotic** • Osmotic laxatives and antacids (e.g., magnesium) • Carbohydrate malabsorption syndromes (e.g., lactose intolerance)	2. **Maldigestion** (loss of digestive function) • Obstructive biliary disease • Bile acid malabsorption • Chronic Pancreatitis	2. **Invasive infections** • Tuberculosis (enteritis) • Clostridium difficile (pseudomembranous colitis) • Amoebiasis • Cytomegalovirus (in immunocompromised)
3. **Functional** (smaller volumes, improves at night and with fasting) • Irritable bowel syndrome		3. **Neoplasms** • Colon cancer • Lymphoma

(Adapted from Gregory Juckett and Rupal Trivedi, American Family Physician, Volume 84, ***Number 10)***

Clinical features and diagnostic approach to adults with chronic diarrhea

- A detailed history is crucial in the assessment of patients with chronic diarrhea.
- The history should focus on establishing the following;
  1. The type of diarrhea: watery, fatty, and inflammatory History and examination: secondary care assessment
  2. Differentiate functional from organic causes
  3. Assess for the specific causes

Table 6.7: Useful clues in the medical history

History	Diagnostic input
• Abrupt onset	○ Suggests infectious causes
• Blood in the stool	○ Inflammatory bowel disease, neoplasms
• Oily(fatty) bulky stool	○ Malabsorption
• Weight loss	○ Organic causes as opposed to functional causes
• Nocturnal diarrhea	○ Organic causes
• Preceding antibiotics	○ Pseudomembranous colitis
• Drugs	○ Possibility of drug side effects
• Significant abdominal pain	○ Mesenteric ischemia, intermittent obstruction,
• Intermittent abdominal pain relived by defecation	○ Irritable bowel syndrome
• History of abdominal surgery	○ Post-surgery (post bowel resection, post cholecystectomy)
• Excessive flatus	○ Carbohydrate malabsorption
• Known systemic illness	○ Diabetes, hyperthyroidism
• Use of sugar replacements (e.g., diabetics)	○ Sorbitol or mannitol associated osmotic diarrhea

Clinical features of major causes of chronic diarrhea in non-HIV patients

- **Irritable bowel syndrome (IBS)**
  - Irritable bowel syndrome (IBS) is a common cause diarrhea.
  - It causes functional diarrhea.
  - IBS causes a symptom complex of crampy abdominal pain, discomfort alleviated by defecation.
  - The diarrhea usually occurs while awake, often following meals and

disappears during sleep.

- ○ The diarrhea is watery or loss.
- ○ Mucus in the stool is also common.
- ○ "Alarm" symptoms such as nocturnal diarrhea, weight loss, or blood in the stool suggest another diagnosis.
- ○ IBS is a diagnosis of exclusion.
- ○ There are criteria which help in the diagnosis of IBS:
  - A. Manning
  - B. Rome IV criteria

Manning criteria for the diagnosis of IBS

- Pain relieved with defecation
- More frequent stools at the onset of pain
- Looser stools at the onset of pain
- Visible abdominal bloating
- Passage of mucus
- Sensation of incomplete evacuation
  - ○ The higher the number of the clinical characteristics, the higher likelihood of IBS.

Rome IV criteria for IBS

- IBS is defined as recurrent abdominal pain, on average, at least one day per week in the last three months, associated with two or more of the following criteria.
  - ○ Related to defecation
  - ○ Associated with a change in stool frequency
  - ○ Associated with a change in stool form (appearance)

- **Infectious cause of chronic diarrhea**
    - Chronic Giardiasis, bacterial infections and tuberculosis should be considered in the differential diagnosis of chronic diarrhea in adults.
- **Inflammatory Bowel Disease (IBD)**
    - IBD encompasses two major disease entities: ulcerative colitis and Crohn disease.
    - IBD causes inflammatory type of diarrhea with blood and pus in the stool.
    - Ulcerative colitis (involving the distal colon and rectum) result in episodes of rectal bleeding, diarrhea, pain, and tenesmus.
    - IBD with extensive colitis is associated with bloody diarrhea, weight loss, fever, and anemia.
    - Crohn disease typically causes an ileitis but later affects the entire gastrointestinal tract. It results in obstruction, abscess collection, perianal fistula, and weight loss.
    - The diagnosis of IBD is usually supported by colonoscopy.
- **Microscopic colitis**
    - Microscopic colitis is characterized by chronic watery (secretory) diarrhea without bleeding.
    - It usually occurs in middle-aged or old adults.
    - The diarrhea is watery, nocturnal diarrhea, and does not decrease with fasting.
    - The clinical course is mainly intermittent.
    - The term microscopic colitis implies that the diagnosis is made by histology. Although colonoscopy appears normal, biopsy from the colon is needed for the diagnosis.
    - It has two histologic types: lymphocytic colitis and collagenous colitis.

- **Malabsorption syndromes**
  - A number of diseases can cause malabsorptive syndrome.
    - Celiac disease (gluten-sensitive enteropathy)
    - Intestinal bypass
    - Mesenteric ischemia
    - Small bowel bacterial overgrowth.
    - Whipple disease, and giardiasis
    - Absent pancreatic enzymes or bile acids can
  - The classic manifestations of malabsorption are pale, oily (fatty), voluminous, foul-smelling stools, and weight loss despite adequate intake.
  - Finding the typical manifestations is relatively uncommon. Many patients may have mild symptoms mimicking IBS.
  - Investigations
- Basic investigation: stool microscopy for pus cells RBCs and parasites, CBC and CRP
- Further investigation depends on the clinical impression from the history and physical examination. Using alarm signs to decide on the further investigations is useful.
- Alarm features
  - Age of onset after age 50 years
  - Nocturnal diarrhea
  - Progressive abdominal pain
  - Rectal bleeding or melena
  - Unexplained weight loss
  - Anemia

  - High CRP
  - Family history of IBD or colorectal cancer
- All patients with any one of the alarm signs need colonoscopy with or without CT scan of the abdomen depending on the presentation. These patients need to be referred to a facility with colonoscopy and imaging service.
- Patients who fulfill criteria for IBS and have no alarm features do not require extensive investigations but require clos follow up for development of additional symptoms.

TREATMENT

- The main stay of treatment of chronic diarrhea is treating the underlying cause.
- Antidiarrheal agents should only be used as symptomatic management and should be avoided in patients with bloody diarrhea, suspected bacterial diarrhea, and pseudomembranous colitis.
  - **Loperamide**
    - Dosing initially 4 mg, PO, followed by 2 mg after each loose stool (maximum: 16 mg/day)
    - Dose should be decreased to minimum required to control symptoms (usual: 4 to 8 mg/day)
    - If improvement is not observed after 10 days of treatment with 16 mg/day, symptoms are unlikely to be controlled.

REFERRAL

- Adult patients with chronic diarrhea, the cause of which is not clearly identified should be referred to a hospital with gastroenterology specialty service.

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6.6 CONSTIPATION

BRIEF DESCRIPTION

- Constipation is difficult to define. In general, it may be defined as infrequent passage of stool.
- It may be caused by either organic or functional disorders.
- A new onset of constipation should be taken as an alarm sign for possible colorectal malignancy; hence investigation for the underlying cause should be performed before resorting to symptomatic treatment.

CLINICAL FEATURES

- Complaint of persistent, difficult, or infrequent, or seemingly incomplete defecation.

INVESTIGATION AND DIAGNOSIS

- Diagnosis is mainly clinical

TREATMENT

OBJECTIVES OF TREATMENT

- Improve symptoms
- Prevent large bowel obstruction

NON PHARMACOLOGIC

- Removal of the underlying cause
- More fiber diet intake

- High residue diet intake
- Increased fluid intake

PHARMACOLOGIC

- **Short term relief of severe constipation**
    - **Magnesium sulfate,** 10-20mg, PO, in a glass of water, preferably before breakfast.
- **For chronic constipation**
    - Treating constipation with laxatives of any type for long period of time is not advisable.
    - All patients with more than acute constipation should be evaluated for colonic cancer.
    - The presence of weight loss, anemia, and anorexia are strong indicators of malignancy.
    - **First line**
        - Bisacodyl, 5 – 10mg, P.O. at night OR 10mg rectally in the morning
    - **Alternatives**
        - Glycerin rectally at night after moistening with water
        - Liquid paraffin, 10ml, P.O. every 8-12 hours as required

FURTHER READING

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2. World Gastroenterology Organization Global Guidelines. Constipation: a global perspective.
3. Arnold Wald. Constipation: Advances in Diagnosis and Treatment. JAMA. 2016;315(2):185-191.

6.7 ANORECTAL DISORDERS

6.7.1 HEMORRHOIDS

BRIEF DESCRIPTION

- Hemorrhoids are the enlargement of veins of the hemorrhoidal plexus in the submucosal space of the anal canal.
- Hemorrhoids can be external or internal depending on whether it is the internal or external plexus that is enlarged.

CLINICAL FEATURES

- Internal Hemorrhoids are painless and often manifest with bright red rectal bleeding (usually with or following bowel movements)
- Prolapse with defecation or other straining activities can also occur
- External hemorrhoids are quite often painful and manifest with a tender swelling at the anal verge

Grading internal hemorrhoids
Grade I - Visualized on anoscopy only
Grade II - Prolapse with defecation or with straining but reduce spontaneously
Grade III - Require the patient to reduce them into their normal position
Grade IV- Irreducible and may strangulate

INVESTIGATIONS AND DIAGNOSIS

- Diagnosis is usually clinical but confirmation needs anoscopy
- Hemoglobin/hematocrit

TREATMENT

OBJECTIVES OF SYMPTOMS

- Relief of symptoms
- Decrease bleeding and prolapse

- Prevent strangulation

NON PHARMACOLOGIC

- Fluid and fiber rich diet
- Sitz bath
- Avoid constipation
- The main stay of treatment for refractory and significantly relapsing hemorrhoids is surgical.

PHARMACOLOGIC

- Rectal suppositories or topical applications
  - **Options**
    - **Bismuth subgallate**, apply BID for five days
    - **Bismuth Subgallate + Bismuth Oxide** + **Peru Balsam+ Zinc oxide**, BID for 5 days
    - **Hydrocortisone acetate** + **Benzyl benzoate**, apply BID for five days
    - **Lidocaine** + **Aluminium acetate** + **Zinc oxide** + **Hydrocortisone**, BID for 5 days

REFERRAL

- Patients with grade IV hemorrhoids need surgery; hence, surgical consultation or referral is needed.

FURTHER READING

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6.7.2 ANAL FISSURE

BRIEF DESCRIPTION

- Anal fissure is a linear tear in the anal mucosa.
- It is a common benign anorectal problem.
- Anal fissure starts with a tear on the skin of the anus which triggers anal pain and bleeding. The tear affects the internal anal sphincter. The sphincter causes spasms, worsening the pain, causing ischemia, and delays healing.
- The cycle repetitive anal pain and bleeding may lead to the development a chronic anal fissure.
- Chronic anal fissure is defined if the fissure persists for more than two months.
- Anal fissure is commonly misdiagnosed as hemorrhoidal disease due to shared signs and symptoms.

CLINICAL FEATURES

- **Symptoms**
  - Anal pain: the hallmark of anal fissure is severe anal pain. The pain is present at rest but is exacerbated by defecation.
  - The anal pain which worsens during defecation persist minutes to hours after defecation.
  - Anal bleeding: although pain is the most common symptom, mild bright red bleeding seen on toilet paper is also a common symptom.
- **Signs**
  - Avoid digital rectal examination in patients suspected of having anal fissure.
  - On inspection anal fissure appears as longitudinal tear in the anoderm.
  - Acute fissure appears as a fresh and superficial laceration.
  - Chronic fissure has raised edges, visible internal anal sphincter (appears

  - white), often accompanied by external skin tags.
  - Visualizing the fissure is not a requirement to establish a diagnosis.

INVESTIGATIONS

- Additional investigations are not required for the diagnosis or management of anal fissures unless another diagnosis is considered.

DIAGNOSIS

- The diagnosis of anal fissure is made on clinical grounds in a patient anal pain exacerbated by defection with bleeding.
- Visualization of the fissure assists in the confirmation of the diagnosis

TREATMENT

OBJECTIVES OF TREATMENT

- Reliving pain
- Promote healing

NON-PHARMACOLOGIC TREATMENT

- **Sitz bath**
  - Warm sitz bath relaxes the anal sphincter and improves blood flow.
  - Immerse the anus in warm water (do not add soap) for 10 -15 minutes 2-3 times per day consistently.
- **Fiber rich diet**
  - Wholegrain based meals: whole barley, whole wheat, peas, beans and pulses.
  - Nuts and seeds.
  - Vegetables: carrots, cabbage, tomato, potatoes with skin
  - Fruits; lemon and oranges such as berries, pears, melon and oranges.

PHARMACOLOGIC TREATMENT

- **Topical analgesics**

- Topical analgesic gel or creams:
    - Topical lidocaine (2%)

      OR
    - Lidocaine containing gels or creams prepared for hemorrhoids gel can be applied for short period of time.
- **Topical vasodilators**
    - If the pharmacy can do compounding, 0.2 – 0.3% nifedipine ointment to be applied BID is a recommended therapy for anal fissure.
- **Laxatives**
    - If there is constipation, laxatives are indicated (see also section on constipation)
        - Bisacodyl 5mg -10mg, PO, once daily

          OR
        - Glycerin adult suppository once daily

          OR
        - Lactulose 15ml twice daily

REFERRAL

- Surgical therapy: Internal sphincterotomy is indicated in patients who persist to have anal fissures despite medical therapy and at low risk of developing fecal incontinence.
- Patients who have indications for surgery needs to be referred to a facility with surgical services.

FURTHER READING

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3. Danielle Davies, Justin Bailey. Diagnosis and Management of Anorectal Disorders in the Primary Care Setting. Prim Care Clin Office Pract 44 (2017) 709–720

6.7.3 PERIANAL (ANORECTAL) ABSCESS

BRIEF DESCRIPTION

- Perianal and perirectal abscesses are common benign anorectal problems.
- Perianal abscess starts from infection of anal glands. The pus collected in the gland tracts in to the adjacent tissue resulting in perianal or perirectal abscess collection.
- Perianal abscesses can also be caused by underlying diseases such as Crohn's disease, tuberculosis, HIV infection, and malignancy.
- Perianal abscesses are classified based on their anatomic location (ischiorectal, Intersphincteric, supralevator, horseshoe). Clinically the location can be classified as superficial or deep.
- Anorectal abscesses and fistulas are considered as a spectrum of the same disease.
- A large proportion of patients with anorectal abscesses will either have a concomitant fistula or develop it later after treatment of the abscesses.
- In addition to fistula formation untreated anorectal abscess can be a focus for severe sepsis.

CLINICAL MANIFESTATIONS

- **Symptoms**
    - **Pain:** severe pain in the anal or rectal area.
    - Constitutional symptoms: fever and malaise are common
    - Pussy discharge: if the abscess starts draining spontaneously or there is a concomitant fistula purulent discharge may be experienced.

- **Signs**
  - **Extern**ally signs of localized infection: perianal area of redness, tenderness, or fluctuation
  - Digital rectal examination: in deeper abscess the external surface could be normal. Digital rectal examination may identify a fluctuant collection and elicit tenderness.

INVESTIGATION

- Imaging: CT scan of pelvis or intra-rectal ultrasound will help localize deeper abscesses which can't be identified on physical examination.

DIAGNOSIS

- The majority of perianal abscesses are diagnosed clinically based on the presence of severe anal or rectal area pain and physical examination findings.
- In patients with deeper abscesses which cannot be palpated externally or digital rectal examination imaging studies are needed.

TREATMENT

OBJECTIVES OF TREATMENT

- Pain relief
- Prevention of systemic and local spread of the infection
- Reduction of the risk of fistula formation

SURGICAL TREATMENT

- The main stay of treatment of anorectal abscess is surgical drainage.
- Once the diagnosis is made surgical drainage should not be delayed.
- Incision should be made closer to the anal verge in order to minimize the length of a potential fistula.
- Concomitant fistulotomy may be done

ANTIBIOTICS

- Antibiotics alone should not be used as a treatment of perianal abscesses.
- After surgical drainage most patients do not require antibiotic. If the patients is immunocompromized, diabetic, has signs of systemic infection or cellulitis, antibiotics need to be prescribed
  - ○ **Amoxicillin-clavulanate** 625mg (500mg Amoxicillin base) PO TID for 10 days

    OR

  - ○ A combination of **Ciprofloxacin** 500mg PO BID and Metronidazole 500mg PO TID for 10 days

REFERRAL

- All patients with perianal abscess should be treated in facilities with general surgery services.
- If surgical service is not available, patients should be referred promptly.

FURTHER READING

1. Ivy H. Gardner, Ragavan V. Siddharthan, Vassiliki Liana Tsikitis. Benign anorectal disease: hemorrhoids, fissures, and fistulas. Annals of Gastroenterology (2020) 33, 1-10.
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6.8 HEPATITIS

6.8.1 HEPATITIS B VIRUS INFECTION

BRIEF DESCRIPTION

- Hepatitis B virus (HBV) is a double-stranded hepatotrophic DNA virus.
- HBV infection is a global health problem. It is estimated that about 650,000 people die annually worldwide from the consequences HBV infection.
- The prevalence of HBV is highest in sub-Saharan Africa and East Asia.
- Though there is no a nationwide epidemiology study, several studies indicate that Ethiopia has a high burden of HBV infection.
- HBV is transmitted by percutaneous or mucosal exposure to infected blood or body fluids (saliva, menstrual, vaginal, and seminal fluids).
- Mother to child (perinatal) transmission is an important route of transmission.
- Transmission within a household, particularly to children is also an important contributor.
- Sexual transmission may occur in those with multiple sex partners.
- The risk of developing chronic infection is 90% following perinatal infection (up to 6 months of age) but decreases to 20–60% between the ages of 6 months and 5 years. Infection in adulthood leads to chronic hepatitis in less than 5% of cases
- HBV infection causes a number of clinical problems: acute hepatitis, chronic hepatitis, liver cirrhosis, hepatocellular carcinoma, and extrahepatic features (e.g., glomerulonephritis, vasculitis)
- Liver cirrhosis and hepatocellular carcinoma are the two major causes of death in patients with chronic HBV infection
- Chronic HBV infection is a dynamic process due to viral replication and the host immune response.

- Taking viral replication status (HBeAg status), HBV DNA level (viral load), alanine aminotransferase (ALT) values and status of liver inflammation, HBV infection is divided into five phases. (See the table 2. below)
- Having evidence of HBV infection does not necessarily indicate liver injury (hepatitis) or the consequences of liver injury (liver cirrhosis and hepatocellular carcinoma).
- A positive HBV surface antigen (HBSAg) is the hall mark of HBV infection while HBV e-antigen (HBeAg) indicates high viral replication (see table 3 below)
- The presence of liver injury (hepatitis) is confirmed by a rise in transaminases (mainly ALT) or imaging/clinical evidence of liver fibrosis and cirrhosis. (For terminologies see table 8 below)

CLINICAL FEATURES

- **Acute infection**
    - Largely asymptomatic
    - Some patients may have features of acute hepatitis: jaundice, nausea, vomiting, fatigue, right upper quadrant pain.
    - Rarely patients may progress to acute liver failure: encephalopathy, ascites, bleeding diathesis
- **Chronic infection**
    - Largely asymptomatic
    - Some patients may have non-specific symptoms which can be intermittent or persistent: fatigue/lack of energy, poor appetite
- **Decompensated Liver Cirrhosis**
    - Nonspecific symptoms: fatigue, weight loss, poor appetite
    - Jaundice
    - Ascites
    - Variceal bleeding

  - ○ Encephalopathy (mild to severe)
  - ○ Bleeding
- **Hepatocellular Carcinoma**
  - ○ Weight loss
  - ○ Hard irregular liver mass

Table 6.8. Important terminologies in the natural history of HBV infection

• Acute HBV infection	○ New-onset hepatitis B infection that may or may not be symptomatic. ○ Diagnosis is based on detection of hHBsAg and IgM antibodies to hepatitis B core antigen (anti-HBc).
• Chronic HBV infection	○ Persistence of HBsAg for six months or more after acute infection with HBV.
• HBeAg seroconversion	○ Loss of HBeAg and development of anti-HBe antibody
• HBsAg seroconversion	○ Loss of HBsAg and development of anti-HBs
• HBeAg reversion	○ Reappearance of HBeAg in a person who was previously HBeAg negative
• Cirrhosis	○ An advanced stage of liver disease as evidenced by imaging or biopsy characterized by: - Extensive hepatic fibrosis - Nodularity of the liver and alteration of liver architecture

Decompensated cirrhosis	○ Clinical complications of cirrhosis become evident - Jaundice - Ascites - Spontaneous bacterial peritonitis - Esophageal varices and bleeding, - Hepatic encephalopathy - Renal impairment

(Adapted and modified from WHO Guidelines for The Prevention, Care and Treatment Of Persons With Chronic Hepatitis B Infection, March 2015)

Diagnosis and diagnostic evaluation

- The diagnosis of HBV infection starts with HBsAg. A validated HBsAg test needs to be used.

- In addition to those suspected of having liver disease, certain group of individuals need routine screening with HBsAg.

    - ○ Pregnant mothers
    - ○ Infants born to infected mothers
    - ○ Health care workers (including health professionals and supporting staff)
    - ○ Hemodialysis patients and organ transplant recipients
    - ○ People with multiple sexual partners and I.V drug users
    - ○ Sexual partners of infected individuals
    - ○ HIV or HCV positive patients

Table 6.9: Phases of chronic HBV infection

HBeAg positive: phase 1 and 2

- **Phase 1: HBeAg positive chronic HBV infection with no evidence of current hepatitis**
  - HBsAg = positive
  - HBeAg = positive
  - HBV DNA = high (usually >107 IU/ml)
  - ALT = normal
  - Liver disease (fibrosis or cirrhosis) = None to mild
  - Old terminology =Immune tolerant
- **Phase 2: HBeAg positive chronic HBV hepatitis HBeAg positive**
  - HBSAg = positive
  - HBeAg = positive
  - HBV DNA = high (104 - 107 IU/ml)
  - ALT = Elevated (persistently or intermittently)
  - Liver disease (fibrosis or cirrhosis) = present (moderate or severe)
  - Old terminology = Immune reactive HBeAg positive

HBeAg negative: Phase 3 and 4

- **Phase 3: HBeAg negative chronic HBV infection with no evidence of current hepatitis**
  - HBsAg = positive
  - HBeAg = negative
  - HBV DNA level: low (<2,000 IU/ml) or undetectable
  - ALT = Normal
  - Liver disease (fibrosis or cirrhosis) = none
  - Previous terminology = Inactive carrier
- **Phase 4: HBeAg positive chronic HBV hepatitis HBeAg positive**
  - HBsAg = positive
  - HBeAg = negative
  - HBV DNA level: high (>2,000 IU/ml)
  - ALT = Elevated (persistently or intermittently)
  - Liver disease (fibrosis or cirrhosis) = present (moderate or severe)
  - Previous terminology = HBeAg negative chronic hepatitis

- **Phase 5: HBsAg-negative phase**
  - HBsAg = negative
  - HBeAg = negative
  - HBV antibodies = positive antibodies to core antigen HBcAg (anti-HBc), with or
  - without antibodies to HBsAg (anti-HBs).
  - ALT = normal
  - Liver disease = none
  - Previous terminology = occult HBV infection

- **The initial evaluation of patients with chronic HBV infections**: Once HBsAg is confirmed the clinical evaluation should include the following.
  - History and physical examination
    - Emphasizing on symptoms of liver disease and features of cirrhosis, family history of hepatocellular carcinoma.
  - Laboratory tests and imaging
    - Phase of HBV infection: HBV DNA level, HBeAg, liver chemistry tests (ALT, AST, Bilirubin, INR, and Albumin), abdominal ultrasound, CBC and evaluation for fibrosis.
    - Non-invasive screening for liver fibrosis: use one of the score available e.g., APRI score
    - **APRI score = (AST ÷ UNL of ALT) x 100 ÷ platelet count (10^9/L).**
      - APRI >0.5 and <=1.5: Significant fibrosis or cirrhosis possible
      - APRI >1.5 and <=2: Likely significant fibrosis, cirrhosis possible
      - APRI >2: Likely cirrhosis
      - Transient elastography (Fibroscan) if readily available
    - **Co-i**nfection: HIV and HCV screening
    - Screening for hepatocellular carcinoma if clinical suspected: If there is liver mass (CT scan of the abdomen with or without alpha fetoprotein)
- **Follow up tests**
  - In patients with chronic HBV but no indications for antiviral therapy, liver injury as well as viral replication can be variable; hence, regular monitoring is required.

- ALT, APRI score, clinical evaluation every 3 months in all patients
- HBeAg initially negative: HBeAg and HBV DNA level every 6 -12 months
- HBeAg positive initially: HBV DNA level every 6 -12 months

- **Upper limits for normal ALT**
  - 30 U/L for men and 19 U/L for women
  - Use the above cut point rather than the highly variable upper normal limits of different laboratories.

TREATMENT

OBJECTIVES OF TREATMENT

- **The main objectives of HBV treatment**
  - Reduce progression to cirrhosis, hepatocellular carcinoma and associated mortality
  - Improve liver fibrosis
  - Preventing acute or subacute liver failure in acute HBV infection
  - Controlling extrahepatic manifestations.
  - Prevention of HBV reactivation.
  - Prevention of mother to child transmission.
- **Intermediate objectives of treatment**
  - Suppression of HBV DNA levels
  - Induction of HBeAg loss, with or without anti-HBe seroconversion
  - Biochemical response = ALT normalization
  - HBsAg loss: optimal goal but rarely achievable

PHARMACOLOGIC TREATMENT

- **Indications for antivirals in chronic HBV infection.**

- Indications are determined based on the presence or absence of cirrhosis, APRI score, ALT, HBV DNA level, and HBeAg.
- The following are the indications;
    - **A.** All patients with cirrhosis (decompensated) and any detectable viral load: Irrespective of ALT and HBeAg status.
    - **B.** If no liver cirrhosis, one of the following is an indication for antiviral treatment
        - HBV DNA > 20,000 IU/ml and elevated ALT (above the UNL): Irrespective of HBeAg status
        - Detectable HBV DNA and APRI score >= 2 or elevated ALT (above UNL): Irrespective of HBeAg status
        - Age above 30, HBeAg-positive and HBV DNA > 2,000: Irrespective `of ALT
        - Co-infection with HIV.
        - Patients with chronic HBV to be started on immunosuppressives.
        - Extra hepatic manifestation

- **Indications for antiviral in acute HBV infection**
    - The presence acute liver failure or fulminant hepatitis with detectable HBV DNA.

ANTIVIRAL CHOICES

- **First line**
    - **Tenofovir** (Tenofovir disoproxil fumarate) (TDF) 300mg, PO, once daily
        - Avoid in patients with GFR <60ml/min

OR

- **Entecavir** 0.5mg, PO, once daily. For patients with decompensated cirrhosis or those with previous exposure to Lamuvidine the dose should be increased to 1mg, daily.

- Entecavir is preferred over Tenofovir in patients age > 60, chronic kidney disease, osteoporosis or steroid use.

- **Alternatives**
  - **Telbuvidine** 600mg, PO, daily.
    - It should only be used when both first lines are not available or in patients with renal impairment when Entecavir is not available.

MONITORING TREATMENT RESPONSE

- HBV DNA: every three months until undetectable then every six months.
- ALT: every three months.
- HBeAg and antibody to HBeAg (anti-HBe): every six months in patients who are HBeAg-positive.
- Monitoring side effects of tenofovir: serum creatinine and phosphate every 3-6 months.

DURATION OF ANTIVIRAL THERAPY

- Most patients require indefinite treatment
- For patients with cirrhosis treatment should be continued indefinitely.
- For patients without cirrhosis: HBeAg seroconversion to negative and development of HBeAb, if initially HBeAg is positive is considered as possible endpoint of treatment.
- For patients without cirrhosis and initially HBeAg is negative, it's only loss of HBsAg which is considered an endpoint but it happens very rarely; hence, treatment is generally indefinite.

TREATMENT IN SPECIAL POPULATION

- **HIV coinfec**tion: All HIV-positive patients with HBV co-infection should start antiretroviral therapy (ART) with Tenofovir (TDF) based regiment

- HCV coinfection: Treatment of HCV with direct-acting antivirals (DAAs) may cause reactivation of HBV**.**
    - Patients fulfilling the standard criteria for HBV treatment should receive treatment.
    - HBsAg-positive patients undergoing HCV treatment with DAA therapy should be given concomitant treatment.
- **Pregnancy:**
    - In all pregnant women with high HBV DNA levels >200,000 IU/ml Tenfovir should be started at 24 -18 weeks of gestation and continue for up to 12 weeks after delivery.
    - Pregnant women already on NA therapy, Tenofovir should be continued, if on another agent it should be switched to Tenfovir.
    - Tenofovir is not contraindicated in breast feeding.

HBV VACCINATION ADULTS

- **Indications for vaccination**
    - Healthcare workers
    - Immune-compromised individuals including HIV
    - Organ transplant recipients
    - Patients on maintenance hemodialysis
    - Children 1-5 years who missed immunization for HBV
    - Sexual partners and close contacts of infected individuals receive three doses of HBV vaccine.
- **Vaccination schedule**
    - Standard schedule: 0, 1, and 6 months.
    - Accelerated schedule: 0, 1 and 2 months.
    - Accelerated schedule, if requested for rapid protection within 48 hour of exposure: 0, 7 and 21 days.

  - After an accelerated course, a booster at one year is recommended.

- **HBV Immunoglobulin**
  - HBV immunoglobulin provides passive immunity.
  - Indications: In individuals who have not been immunized or have not completed the immunization and have the one of the following indications
    - Perinatal exposure of an infant born to a HBsAg positive mother within 24 hours.
    - Percutaneous or mucosal exposure to HBsAg-positive blood preferably within 24-48 hr.
    - Sexual exposure to an HBsAg-positive person

REFERRAL

- Patients with HBSAg positivity with or without elevated transaminases or evidence of chronic liver disease need evaluation for indications of therapy i.e. HBeAg status, HBV DNA level; hence, they should be referred to a facility where they get access to these tests.

FURTHER READING

1. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. Journal of Hepatology 2017 vol. 67: 370–398
2. Federal Democratic Republic of Ethiopia National Guideline for Prevention and Control of Viral Hepatitis in Ethiopia. FMOH 2016.
3. WHO Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection March 2015. ISBN 978 92 4 154905 9

6 .8.3 HEPATITIS C VIRUS INFECTION

BRIEF DESCRIPTION

- The hepatitis C virus (HCV) is a small, RNA-enveloped virus with a highly variable genome.

- It has multiple genotypes and sub genotypes.
- There are currently seven genotypes identified with variable geographic distribution
- HCV is prevalent in Ethiopia and the commonest genotypes are genotype 4 (60%), followed by gentotype 1(20%).
- Risk factors for acquiring HCV: blood transfusion, IV drug use, cut or injury by bloody object, ear piercing or tattoing
- Hepatitis C virus can cause acute and chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma.
- HCV can also cause a number of extrahepatic manifestations: Glomerulonephritis, vasculitis, thyroiditis, Sjögren syndrome, increase diabetes, porphyria cutanea tarda and lichen planus.
- Male gender, age above 40 or advanced age during infection, alcohol intake, HBV or HCV coinfection, fatty liver and obesity increase the risk of liver cirrhosis.

CLINICAL FEATURES

- Majority of patients with chronic HCV are asymptomatic
- Features of chronic hepatitis: nonspecific symptoms such as fatigue, poor appetite weight loss, jaundice.
- Extrahepatic manifestations: clinical feature depend on the individual manifestation.

DIAGNOSIS AND INVESTIGATION

- **Whom to screen for HCV?**
  - Pregnant women
  - Patients with liver disease
  - Individuals with HBV and HCV infection
  - Commercial sex workers and prisoners

  - Individuals with risk of acquiring infection (e.g.IV drug use, tattooing, body piercing)
- **Screening test**
  - Serum anti-HCV antibody rapid test or enzyme immunoassay EIA (ELISA)
  - In the case of suspected acute hepatitis C, in immunocompromized patients and in patients on hemodialysis, HCV RNA testing can be done as an initial test.
- **Confirmatory test**
  - If anti-HCV antibodies are detected, HCV RNA should be determined by a sensitive molecular method with a lower limit of detection ≤15 IU/ml) to confirm the diagnosis.
  - If anti-HCV antibody-positive, HCV RNA-negative individuals, HCV RNA levels should be repeated after 6 -12 months, to confirm past infection.
- **Investigations before initiation of treatment**
  - Complete blood cell count (CBC)
  - Liver enzymes and function test (AST, ALT, ALP, Bilirubin, ALB and INR)
  - Serum Creatinine, BUN
  - Quantitative HCV RNA (IU/ml)
  - Pregnancy test for reproductive age group women.
  - HIV and HBV screening
- **Optional tests**
  - Genotyping
  - Abdominal Ultrasonography
- **Assessing the degree of liver fibrosis and cirrhosis**: see in HBV
- **Screening for hepatocellular carcinoma if clinical suspected and**

there is liver mass on ultrasound: CT scan of the abdomen with or without alpha fetoprotein.

TREATMENT

OBJECTIVES OF TREATMENT

- To eradicate HCV RNA (attainment of a sustained virologic response (SVR).
- SVR is defined as an undetectable HCV RNA level after 12 weeks of therapy.
- Who should be **treated with direct acting antivirals (DAA)?**
    - All patients with HCV infection, who are willing to be treated, should be treated.
    - Treatment should be started without delay in patients with significant fibrosis or cirrhosis, including decompensated cirrhosis; patients with clinically significant extra-hepatic manifestations.
- **Which agent to use?**
    - A simplified, pangenotypic anti-HCV treatment is preferred.
    - Pre-treatment assessment can be limited to proof of HCV.
- **First line pangenotypic regimen**
    - **Sofosbuvir/velpatasvir** combination (400 mg of sofosbuvir and 100 mg of velpatasvir), one tablet once daily for 12 weeks.
- **Alternative regimen**
    - **Sofosbuvir** 400 mg oral once daily **+ Daclatasvir 60mg** oral once daily for 12 weeks
- **Treatment monitoring**
    - HCV RNA at baseline, at the end of therapy (12 weeks) and after completion of treatment.
    - Toxicity of concurrent drugs given for comorbidities and potential drug-drug interactions should be monitored.

REFERRAL

- All patients with HCV should be offered treatment.Those with liver disease or extrahepatic manifestations should be treated more urgently. Hence, all patients should be referred to facility where HCV treatment and follow is provided. Those who need urgent treatment should be referred without delay.

6.8.4 ACUTE LIVER FAILURE AND FULMINANT HEPATITIS

BRIEF DESCRIPTION

- Acute liver failure (ALF) refers to the rapid development of severe acute liver injury with impaired synthetic liver function and hepatic encephalopathy in a person who previously had a normal liver or well-compensated liver disease.
- Fulminant hepatitis (FH) refers to the development of hepatic encephalopathy within eight weeks of the onset of symptoms in a patient with a previously healthy liver or the appearance of encephalopathy within two weeks of developing jaundice.
- Causes of ALF or FH are similar to that of acute hepatitis.

CLINICAL FEATURES

  - Jaundice
  - Bleeding
  - Ascites and edema
  - Hepatic encephalopathy-depressed mental status, restlessness
  - Decreased urine out put
- **Investigations-**see acute hepatitis

TREATMENT

- Patients should be treated in an ICU setting.

- Secure air way, IV-line, correct hypoglycemia and hypotension, insert NG tube if unconscious
- Catheterize the urinary bladder and refer to a referral with ICU facilities.

REFERRAL

- All patients should be referred to facility where there is ICU

6.9 LIVER CIRRHOSIS AND PORTAL HYPERTENSION

BRIEF DESCRIPTION

- Cirrhosis represents a late stage of progressive hepatic fibrosis with distortion of the architecture of the liver with formation of regenerative nodules.
- It can result from any cause of chronic liver disease e.g., chronic viral hepatitis, alcoholic liver disease.
- Patients with cirrhosis develop a variety of complications which cause marked morbidity and mortality.
- The common complications include ascites, spontaneous bacterial peritonitis, variceal bleeding, hepatic encephalopathy, hepatorenal syndrome and hepatocellular carcinoma.

CLINICAL FEATURES

- **Symptoms**
  - Symptoms of cirrhosis are generally nonspecific (fatigue, poor appetite, weight loss)
  - Symptoms of complication e.g., body swelling, hematemesis or melena
- **Signs**
  - Liver and spleen may be enlarged
  - Scleral icterus

  - Parotid gland enlargement
  - Palmar erythema, spider angiomas
  - Pubic and axillar hair loss
  - Ascites and edema
  - Sleep disturbance, behavioral or mental status changes in patients with encephalopathy

INVESTIGATIONS

- Ultrasound is important in assisting the diagnosis of cirrhosis
- CBC: Thrombocytopenia is an important maker
- Transaminases (ALT and AST): might be normal in advanced cirrhosis
- Bilirubin
- INR and Serum Albumin
- Upper GI endoscopy
- Creatinine and Urea, serum electrolytes

DIAGNOSIS

- No single laboratory test is diagnostic of liver cirrhosis accurately.
- The diagnosis is made based on combination of clinical findings (history and physical examination), indicators of decreased synthetic liver functions (elevated INR or PT and/or low serum albumin), low platelets and ultrasound findings.

TREATMENT

OBJECTIVES OF TREATMENT

- Reduce complication rates
- Treating the complications
- Decrease hospitalization

NON PHARMACOLOGIC

- Salt restriction (< 2 g/day)-for ascites
- Monitor weight regularly
- Bed rest
- Low protein diet-for encephalopathy
- Endoscopic sclerotherapy and/or banding-for variceal bleeding

PHARMACOLOGIC TREATMENT

I. For ascites/edema

- **First line**
    - **Spironolactone**
        - Starting dose 100 mg/day in single or two divided doses
        - If there is no response, increase doses every 3-7days (in 100 mg steps)
        - Maximum dose 400mg/day
        - Serum potassium should be checked regularly: at start, at dose increments and on each follow up visit
- **Add-on or alternative**
    - **Furosemide**
        - Ass add-on: in patients who do not respond to spironolactone (body weight reduction less than 2 kg in one week)
        - As an alternative: in patients who have hyperkalemia or impaired kidney function at baseline or develop later
        - Starting dose from: 20mg, BID
        - Increments by 40mg/day
        - Maximum dose for this indication: 160 mg/day (80mg BID)

II. Encephalopathy

- **Lactulose,** 10–30mL PO (Via NG tube) 8 hourly. Aim for 2 soft stools / day and no diarrhea

  PLUS

- **Metronidazole**, 250mg, PO every 8 hour

III. Esophageal varices-prevention of variceal bleeding (Both primary and secondary)

- **Propranolol,** 20mg – 40mg, PO, two to three times daily start low dose and escalate gradually.

IV. Spontaneous bacterial peritonitis

- **Treatment of Spontaneous bacterial peritonitis**
  - First line: Ceftriaxone, 1000mg, IV, BID for 7-10 days
  - Alternative: Ciprofloxacin, 200mg, IV, BID for 7-10 days
- **Prophylaxis for spontaneous bacterial peritonitis (SBP)**
  - Indications to start prophylaxis
    - Patients who recover from an episode of SBP
    - Advanced cirrhosis and ascitic fluid protein lower than 1.5 g/dl without prior SBP
    - In patients with gastrointestinal bleeding and severe liver disease
  - First line: Norfloxacin, 400mg, P.O. daily
  - Duration of prophylaxis: Generally indefinite but if there is long-lasting improvement with disappearance of ascites, prophylaxis can be discontinued.

FURTHER READING

1. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. Journal of Hepatology 2018 vol. 69: 406–460.
2. Grattagliano I, Ubaldi E, Bonfrate L, Portincasa P. Management of liver cirrhosis between primary care and specialists. World J Gastroenterol

2011; 17(18): 2273-2282

3. Smith A, Baumgartner K, Bositis C. Cirrhosis: Diagnosis and Management. Am Fam Physician. 2019 Dec 15;100(12):759-770.
4. Christopher Fowler. Management of patients with complications of cirrhosis. 4 The Nurse Practitioner;Vol. 38, No. 4.

6.10 CHOLELITHIASIS (GALL STONES) AND CHOLECYSTITIS

6.10.1 CHOLELITHIASIS (GALL STONES)

BRIEF DESCRIPTION

- Gallstones are common clinical problem encountered in adult primary care practice.
- The majority of gall stones are cholesterol stones and a small proportion are pigment stones. Pigment stones are common in patients with hemolytic anemia or cirrhosis.
- Gallstones originate from the complex interaction of genetic, environmental, local, systemic and metabolic abnormalities
- Most individuals with gallstones are asymptomatic and will remain so throughout their lives.
- The major complications of gall stones are cholecystitis, choledocholithiasis with or without acute cholangitis, and pancreatitis.
- When gall stones start to cause symptoms, it is called gallstone disease.
- Uncomplicated gallstone disease refers to gall stone disease associated with biliary colic but no other complications such as acute cholecystitis, cholangitis, or gallstone pancreatitis.
- Among patients who develop symptoms, a significant number will subsequently develop complications
- As both upper gastrointestinal symptoms and gall stones are common

problems, finding of gall stones on abdominal ultrasound in patients having non-specific symptoms creates confusion on whether the symptoms are due to the gall stones or not.

- Differentiating patients with asymptomatic gall from those with symptomatic gall stones is crucial since cholecystectomy is often curative in symptomatic gallstones, but it exposes those with incidental gallstones to unnecessary surgical risk.

CLINICAL FEATURES

- Symptoms
- Asymptomatic: the cast majority of patients are asymptomatic.
- Bi**liary** colic
  - ○ Severe, dull, right upper quadrant or epigastric or substernal pain.
  - ○ It is usually constant (contrary to the name, it is not usually colicky).
  - ○ It is often associated with sweating, nausea, and vomiting.
  - ○ It may radiate to the back (particularly to the right shoulder)
  - ○ The pain stays at least 30 minutes, plateaus within an hour then subsides. The entire attack usually lasts less than six hours.
  - ○ Eating a fatty meal is a common trigger
- **Atypical symptoms**
  - ○ Several symptoms, other than biliary colic, have been attributed to gall stones. However, there association with gallstones is poor.
  - ○ These include non-specific abdominal pain epigastric burning pain, retrosternal burning pain, chest pain, nausea or vomiting, belching, abdominal bloating, and early satiety.

SIGNS

- There are physical signs in patients with asymptomatic gallstones.
- In patients with biliary colic the abdomen is generally non-tender with no

signs of peritonitis

DIAGNOSIS AND INVESTIGATIONS

- Abdominal ultrasound: is the gall standard tool for the diagnosis of cholelithiasis.
- Additional investigations are generally unnecessary unless other diagnoses are considered.
- Once diagnosis is made clinical categorization of patients is helpful for decision making. The following categorization is found to be useful.
    - **Category 1**: Incidental gallstones: Asymptomatic, incidental finding on imaging.
    - **Category 2**: Uncomplicated gallstone disease: symptomatic with typical biliary colic and gallstones on imaging but no evidence of complications.
    - **Category 3**: Atypical symptoms and gallstones on imaging studies
    - **Category 4:** Typical biliary symptoms but without gallstones on ultrasound

TREATMENT

OBJECTIVES OF TREATMENT

- Pain relief
- Prevention of complications

PHARMACOLOGIC AND SURGICAL TREATMENT

- **Treatment of biliary colic**
    - **Pain management:** the preferred agents are parenteral NSAIDS
        - Diclofenac 50-75mg IM or IV stat
        - If NSAIDS are contraindicated (e.g., impaired kidney function or hypersensitivity) opioids can be used: Morphine 2.5 -5mg IV stat or Pethidine 50mg IV stat.

- **Surgery**: The main stay of treatment is surgery (Cholecystectomy).
- Indications for cholecystectomy based on patient categorization.
    - **Category 1:** Incidental gallstones: not indicated
    - **Category 2:** Uncomplicated gallstone disease: indicated.
    - **Category 3**: Atypical symptoms: look for other causes for the symptoms and individualize surgical decision.
    - **Category 4:** Typical biliary symptoms but on gallstones on ultrasound: follow up and individualize surgical decision.

FURTHER READING

1. EASL Clinical Practice Guidelines on the prevention, diagnosis and treatment of gallstones. J Hepatol (2016), http://dx.doi.org/10.1016/j.jhep.2016.03.005
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3. Sherly Abraham; Haidy G. Rivero; Irina V. ERLIKH et al. Surgical and Nonsurgical Management of Gallstones. *Am Fam Physician*. 2014;89(10):795-802

6.10.2 ACUTE CHOLECYSTITIS

BRIEF DESCRIPTION

- Acute cholecystitis refers to inflammation of the gallbladder.
- It commonly develops as a complication of gallstones, called calculous cholecystitis (acute cholecystitis).
- Less often it can occur in the absence gallstones, called acalculous cholecystitis.
- Occasionally cholecystitis may occur over a long period of time or may be discovered during cholecystectomy done for symptomatic gall stones, this is called chronic cholecystitis).

- Acute cholecystitis can complicate with sepsis, generalized peritonitis (perforation), or bowel obstruction (gallstone ileus).

CLINICAL MANIFESTATIONS

- **Symptoms**
  - Abdominal pain
    - Severe right upper quadrant or epigastric pain.
    - The pain is usually steady and prolonged (more than 4 – 6 hours), steady
    - History of preceding fatty food ingestion is common.
  - Fever
  - Nausea, vomiting and anorexia
- **Signs**
  - Acutely sick looking general appearance and lie still.
  - Fever
  - Tachycardia
  - Abdominal findings
    - Localized right upper quadrant tenderness
    - Voluntary and involuntary guarding
    - Patients frequently will have a positive Murphy's sign.
    - Murphy's **sign**
      - ✓ Patients with acute cholecystitis frequently have a positive Murphy's sign".
      - ✓ Check for Murphy's sign: ask the patient to inspire deeply while your hand palpates the area of the gallbladder fossa just beneath the liver edge.
      - ✓ Worsening of the pain during deep inspiration is

considered as a positive Murphy’s sign.

INVESTIGATIONS

- CBC
- Liver enzymes (AST, ALT, Alkaline phosphatase) and serum bilirubin.
- Abdominal ultrasound

DIAGNOSIS

- The diagnosis of acute cholecystitis should be suspected patients presenting with acute abdominal pain, fever, leukocytosis
- Ultrasound of the abdomen is needed to confirm the diagnosis: it shows gallbladder wall thickening or edema and/or sonographic Murphy’s sign.
- Severity grading of acute cholecystitis: see the table below for the Tokyo guidelines on severity grading of acute cholecystitis

Table 6.10: Tokyo guidelines (TG) TG18/TG13 severity grading for acute cholecystitis

Grade I (mild) acute cholecystitis 1. “Grade I” acute cholecystitis does not meet the criteria of “Grade III” or “Grade II”. 2. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure.
Grade II (moderate) acute cholecystitis Acute cholecystitis is associated with any one of the following conditions: 1. Elevated WBC count (>18,000/mm3) 2. Palpable tender mass in the right upper abdominal quadrant 3. Duration of complaints >72 ha 4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis

Grade III (severe) acute cholecystitis

Acute cholecystitis is associated with dysfunction of any one of the following organs/systems:

1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥5 lg/kg per min, or any dose of norepinephrine
2. Neurological dysfunction: decreased level of consciousness
3. Respiratory dysfunction: PaO2/FiO2 ratio <300
4. Renal dysfunction: oliguria, creatinine >2.0 mg/dl
5. Hepatic dysfunction: PT-INR >1.5
6. Hematological dysfunction: platelet count <100,000/mm3

Ref. J Hepatobiliary Pancreat Sci (2018) 25:41–54

TREATMENT
OBJECTIVES OF TREATMENT

- Pain relief
- Prevent development of complications

PHARMACOLOGIC AND NON-PHARMACOLOGIC TREATMENT

- Admission: Patients with acute cholecystitis should be admitted,
- Rest the bowel: keep patients NPO until symptoms subside.
- Intravenous fluids: see section on IV fluid therapy
- Pain management:
  - Parenteral NSAIDS are the preferred agents for pain management e.g., Diclofenac 50 -75mg IV/IM every 12 hours.
  - Opioids should be reserved for patients with contraindications to NSAIDS (e.g., renal impairment or hypersensitivity). Morphine 2.5 -5 mg, IV or pethidine 50mg, IV.

- **Antiemetic**
    - Metoclopramide 10mg IV 8- 12 hours
- **Antibiotics**
    - Ceftriaxone 1gm IV, BID PLUS Metronidazole 500mg IV TID 7 – 10 days
- **Alternative**
    - Ciprofloxacin 200 - 400mg IV BID PLUS Metronidazole 500mg IV TID 7 -10 days
- **Cholecystectomy**
    - Cholecystectomy is indicated in patients who have or had acute cholecystitis
    - The timing of the surgery depends on the patient's clinical status; in patients who have low risk for general anesthesia/surgery, cholecystectomy can be done during the same hospitalization. In others interval cholecystectomy can be done.
    - In patients with worsening clinical condition or complication of acute cholecystitis emergency surgery is indicated.

REFERRAL

- Patients with acute cholecytitis should be admitted and treated in a health facility with surgical services.

FURTHER READING

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6.11 LIVER ABSCESS

6.11.1 PYOGENIC LIVER ABSCESS

BRIEF DESCRIPTION

- Pyogenic liver abscess is a localized suppurative infection of the liver. It could be single or multiple. It is the most common type of visceral abscess.
- Diabetes, underlying hepatobiliary disease and gastrointestinal malignancy are the major risk factors for the development of pyogenic liver abscess.
- Pyogenic liver abscesses mainly arise following one or more episodes of bacteria seeding in to portal circulation rarely systemic hematogenous sources cause pyogenic liver abscesses.
- Most pyogenic liver abscesses are polymicrobial intestinal anaerobes and gram negatives predominate, however, the microbiology can be variable in different settings.

CLINICAL MANIFESTATIONS

- **Symptoms**
    - Abdominal pain: localized right upper quadrant pain
    - Fever
    - Other symptoms: nausea and vomiting, anorexia, weight loss
- **Signs**
    - Hepatomegaly
    - Right upper quadrant tenderness,
    - Jaundice

DIAGNOSIS

- Clinical suspicion of pyogenic liver abscess starts with history and physical examination.
- Confirmation of the diagnosis requires imaging studies (ultrasound or

CT scan of the abdomen) and image guided aspiration for microbiologic studies.

- The most important differential diagnosis is amebic liver abscess. Both ultrasound and CT scan can't reliably differentiate pyogenic liver abscess from amebic liver abscess.
- The aspirate take using ultrasound or CT guidance should be sent for gram stain, culture (both aerobic and anaerobic culture). Anaerobic culture needs to be requested specifically as it is not routinely done.
- Investigations
- Imaging: ultrasound of the abdomen. CT scan can also be used
- Image (ultrasound or CT scan) guided aspirate gram stain and culture.
- Other laboratory test: CBC, Liver enzymes and bilirubin,

TREATMENT

OBJECTIVES OF TREATMENT

- Attain complete resolution of the abscess.

Pharmacologic and non-pharmacologic treatments

- There are two lines of treatment in the management of pyogenic liver abscess: drainage of the abscess and antibiotic therapy.

  1. **Drainage of abscess**: Drainage can be attained by two mechanisms either ultrasound-guided or surgical drainage. The choice depends on the size and number of abscesses.

- **Single a**bscesses with a diameter ≤5 cm: ultrasound guided percutaneous catheter drainage or needle aspiration is acceptable
- Single abscesses with diameter >5 cm: ultrasound guided catheter drainage, needle drainage is not adequate. The drainage catheter should be kept until the drainage is minimal.
- Surgical drainage is usually preferred in the following circumstances:
  - Multiple abscesses

  - o Multi-loculated abscesses
  - o Failed catheter drainage: no improvement in the first week or if the drainage catheter is blocked by thick pus.

2. Antibiotics

- Empiric IV antibiotics should be started while awaiting culture results.
  - – First line: Ceftriaxone 1gm IV, BID PLUS Metronidazole 500mg IV TID
  - – Alternative: Ciprofloxacin 400mg IV BID PLUS Metronidazole 500mg IV TID
    - o Duration of antibiotic therapy 4 - 6 weeks. If there is a good response antibiotic can be changed to oral after 2 – 4 weeks. Empiric oral antibiotic options:
  - – Amoxicillin-clavulanate 625mg PO TID

    OR
  - – Ciprofloxacin 500mg PO BID Plus Metronidazole 500mg PO TID

REFERRAL

- Patients with pyogenic liver abscess should be treated in a facility with surgical service and facilities for percutaneous image guided drainage.

FURTHER READING

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6.11.2 AMEBIC LIVER ABSCESSES

BRIEF DESCRIPTION

- Most Entamoeba histolytica infestations are asymptomatic. Among symptomatic presentation amebic colitis (amebic dysentery) is the commonest presentation.

- Rarely the trophozoite rarely invades the intestinal mucosa and spreads hematogenous. This spread may result in extra intestinal manifestation.
- The most common extraintestinal manifestation is amebic liver abscess.
- Men are more commonly affected than women.
- The most common complication of amebic liver abscess is rupture. Depending on the location of the abscess the rupture can be in to the peritoneum, pleural space, pericardial space, or cause sub-phrenic space.

CLINICAL MANIFESTATIONS

- **Symptoms**
  - Right upper quadrant pain: subacute or long standing right upper quadrant abdominal pain.
  - Fever
  - Nausea/vomiting
  - Anorexia
  - Associated diarrhea: not common (less than one-third)
  - Jaundice: rarely seen (in less than 10%)
- **Signs**
  - Right upper quadrant tenderness
  - Hepatomegaly
  - Signs of pleural effusion

DIAGNOSIS

- The diagnosis of amebic liver abscess requires imaging study.
- Ultrasound is commonly used due to its wide availability. CT scan of the abdomen can be used. However, imaging finding cannot reliably differentiate amebic liver abscess from pyogenic liver abscess.

- Amebic liver abscess is usually single and located in the right lobe of the liver.
- Aspiration is not generally needed for diagnosis. If aspirated, it appears a brown, thick fluid.

INVESTIGATIONS

- Abdominal ultrasound
- CBC
- Liver enzymes
- Stool microscopy: usually negative but finding of a trophozoite can be helpful

TREATMENT

OBJECTIVE OF TREATMENT

- Attain resolution of abscess
- Prevent complications
- Phar**macologic and non-pharmacologic treatment**
    - **Antimicrobial treatment (tissue agent)**: the main stay of treatment of amebic liver abscess is antimicrobial therapy.
        - **Metronidazole** 500-750 mg IV/PO every 8 hour for 7-10 days

          OR
        - **Tinidazole** 2 g PO daily 3-5 days
    - **Follow up antimicrobial (luminal agent)**: After completing either metronidazole or Tinidazole as above either of the following luminal agents can be used
        - **Diloxanide furoate 500 mg every 8 hours 10 days**

          OR
        - **Paromycin** 25-30 mg/kg PO per day in 3 divided doses 7 days

- **Drainage**
  - Drainage is not routinely recommended.
  - Percutaneous ultrasound guided drainage may be considered in patients with large amebic liver abscess > 10cm in diameter or imminent rupture and those with failed medical therapy.

FURTHER READING

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2. Christoph Lübbert, Johannes Wiegand, Thomas Karlas. Therapy of Liver Abscesses. Viszeralmedizin 2014; 30:334–341. DOI: 10.1159/000366579
3. Trillos-Almanza MC, Restrepo Gutierrez JC. Frontline Gastroenterology 2020; 0:1–7.

6.12 ACUTE PANCREATITIS

BRIEF DESCRIPTION

- Acute pancreatitis is an acute inflammation of the pancreas.
- There are a number causes for acute pancreatitis. The leading causes are gallstones and chronic alcohol abuse. The other less common causes are hypertriglyceridemia, hypercalcemia, drugs, and infections such as mumps, smoking and trauma.
- Acute pancreatitis should be suspected in any patient with acute abdominal pain.
- It is associated with development of local complications (necrosis, pseudocyst), sepsis, multi-organ dysfunction and mortality.
- Acute pancreatitis is divided in to three severity classes based on the presence of organ dysfunction and mild complication.
  - **Mild acute pancreatitis:** No organ failure and local or systemic complications

  - **Moderately severe acute pancreatitis:** transient organ failure (resolves within 48 hours) and/or local or systemic complications without persistent organ failure (>48 hours)
  - **Severe acute pancreatitis**: persistent organ failure, one or more.

CLINICAL FEATURES

- **Symptoms**
  - Abdominal pain: acute, severe, persistent epigastric or right upper quadrant, rarely left side abdominal pain. The pain usually radiates to the back.
  - Nausea and vomiting.
  - Fever
  - Shortness of breath.
- **Signs**
  - **Tenderness:** epigastric tenderness, severity depends on the severity of the pancreatitis/
  - **Deranged vital signs**: Fever, tachycardia, hypoxia, or low blood pressure.
  - **Signs of the underlying disease**: e.g., parotid swelling in mumps.

Investigation

- **Serum amylase and lipase**
  - Elevated in the majority of patients
  - Lipase is more specific than serum amylase.
  - Significant elevation is considered when they are elevated more than three times the upper limit of normal.
- CBC, CRP
- Liver enzymes (ALT, AST, ALP, Bilirubin)

- BUN and creatinine.
- Serum electrolytes
- Abdominal ultrasound: useful but is less sensitive than CT scan. Ultrasound can detect causes like gallstones and complication like pseudocyst.
- Abdominal CT scan: the imaging choice for the diagnosis of acute pancreatitis.

DIAGNOSIS

- The diagnosis of acute pancreatitis requires the presence of two of the following
    - Acute onset of severe, persistent epigastric pain often radiating to the back
    - Elevation in serum lipase or amylase at least three times the upper limit of normal.
    - Characteristic imaging findings of acute pancreatitis: CT scan or abdominal ultrasound.

TREATMENT

OBJECTIVES OF TREATMENT

- Pain control
- Fluid, electrolyte, and nutritional abnormality prevention and correction
- Management of complications
- Treatment
- The main stay of treatment of acute pancreatitis is supportive.
- Admission to the ICU: patients with severe and moderately severe pancreatitis need follow up and treatment in ICU.
- Fluid and electr**olyte correction**
    - Avoid volume depletion (adequate fluids with Ringer's Lactate).
    - Give Ringer's lactate or Normal saline (see section on intravenous fluids)

- **Feeding and nutrition**
    - Start early (within 24 hours) oral re-feeding
    - Early feeding may not be successful in all patients due to abdominal pain, vomiting, or ileus. In such patients feeding may need to be delayed beyond 24 hours
    - In those who do not tolerate early feeding, try to restart as soon as possible.
- **Pain control**
    - Opioids: Morphine IV, 1-3 mg every 4 hour OR Pethidine 25-100 mg SC or IM
    - Paracetamol 500-100mg every 6 -8 hour.
    - Avoid NSAIDS such as Diclofenac.
- **Antiemetics**
    - Metoclopramide 10 mg IV/IM every 8 hours
- **Antibiotics:** indicated in patients with evidence of infected pancreatic necrosis
    - Infected pancreatic necrosis: evidenced based by clinical deterioration, increasing WBC count, fevers or fail to improve after 7 to 10 days of hospitalization.
    - Prophylactic antibiotics are not indicated
- **NG tube insertion for suction**
    - When there is evidence of paralytic ileus or persistent vomiting

REFERRAL

- Patients with acute pancreatitis need to be managed in a hospital with ICU facilities.

FURTHER READING

1. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. Gastroenterology 2018; 154:1096–1101
2. Ari Leppäniemi, Matti Tolonen, Antonio Tarasconi et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World Journal of Emergency Surgery (2019) 14:27. https://doi.org/10.1186/s13017-019-0247-0
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CHAPTER 7:

HEMATOLOGIC DISORDERS

7.1 NEMIA

7.1.1 APPROACH TO ADULTS WITH ANEMIA

BRIEF DESCRIPTION

- Anemia is functionally defined as reduction in red blood cell (RBC) mass, accompanied by a decrease in oxygen carrying capacity.
- Laboratory wise anemia is defined as a reduction in one or more of the three RBC measurements in the CBC: hemoglobin (Hg), hematocrit (HCT), or RBC count. For practical purposes, hemoglobin or hematocrit are commonly used.
- WHO criteria for diagnosing anemia in men and women are hemoglobin values <13 and <12 g/dl, respectively.
- Anemia is not a single disease entity; it is rather a manifestation of several pathologies.
- Anemia can be classified based on RBC morphology (size), as measured by mean corpuscular volume (MCV).
- Classification based on of RBC size is useful for considering possible causes; however, it should never be taken as diagnostic.
    - Microcytic: MCV<80 fl
        - Common causes: iron deficiency anemia and anemia of chronic disease
    - Normocytic: MCV 80-100 fl

    - Common causes: anemia of chronic disease, CKD
  - Macrocytic: MCV> 100 fl
    - Common cause: vitamin B12 deficiency, alcohol abuse, chronic liver disease
- Base on the cause, anemia can be divided in to two broad categories:
  - Anemia due to increased RBC loss or destruction
    - Hemorrhage
    - Hemolysis
- Anemia due to defective or decreased RBC production
  - Iron deficiency anemia
  - Vitamin B12 or folate deficiency
  - Anemia of chronic disease
  - Chronic kidney disease
  - Hypothyroidism,
  - Aplastic anemia
  - Bone marrow infiltration: Leukemia, lymphomas, other cancers, granulomatous diseases
  - Chemotherapy induced anemia

CLINICAL FEATURES

Symptoms

- Fatigue, dyspnea, palpitation, syncope
- Headache, lightheadedness, tinnitus, vertigo, difficulty of concentration
- Anorexia, nausea, indigestion
- Symptoms s of the underlying disease e.g., melena in GI bleeding, heavy menstrual bleeding, generalized body swelling in CKD

Signs

- Pallor, tachycardia, wide pulse pressure /ejection systolic murmur.
- Signs of Heart Failure (raised JVP, S3, hepatomegaly, edema)
- Signs of the underlying disease-causing anemia: lymphadenopathy, splenomegaly, angular chelitis, tumors (abdominal/ pelvic mass) etc.
- Investigation and diagnosis
- CBC with RBC indices
- Peripheral blood smear
- Reticulocyte count and index
- Further investigations: depends on the suspected cause/s of anemia based on the above tests, the history and physical examination findings.
    - **Suspected iron deficiency anemia**: serum ferritin, total iron binding capacity (TIBC), transferrin saturation ([serum iron ÷ TIBC] X 100%)
    - **Once iron deficiency is diagnosed**: stool for occult blood, stool microscopy for hookworm infestation, upper GI endoscopy or colonoscopy may be needed based on the clinical suspicion.
    - **Suspected megaloblastic anemia**: serum vitamin B12 level, serum folate and if serum folate level is normal.
    - **Suspected hemolytic anemia**: Reticolcultye count or percenetage bilirubin (indirect hyperabuleminmia), LDH, Coomb's test.

TREATMENT
OBJECTIVES OF TREATMENT

- Improve the functional status of the patient by correcting the hemoglobin.
- Treatment of the underlying cause

NON PHARMACOLOGIC

- Transfusion of packed RBC: Indications for transfusion
    - Hemoglobin $\leq$ 7g/dl: for most hospitalized medical or surgical patients

  - For ambulatory patients with chronic anemia transfusion may not be needed even at hemoglobin is <7g/dl, unless the patients have severe symptoms e.g., heart failure
  - Hemoglobin < 8g/dl: for those with pre-existing chronic cardiac disease, undergoing orthopedic or cardiac surgery
  - In trauma or acutely bleeding patients
    - Do not use hemoglobin or hematocrit for transfusion decision as they are falsely elevated
    - Hemodynamic status and ongoing nature of bleeding should be used
    - Whole blood is preferable if there is acute or ongoing bleeding
  - For the following patients higher hemoglobin target might be aimed
    - Acute coronary syndrome
    - Severe thrombocytopenia in hematology/hematology patients
- Nutritional support
- Non pharmacologic treatment pertinent to the underlying cause

PHARMACOLOGIC

- Pharmacologic treatment depends on the underlying cause of anemia.

REFERRAL

- Patients with anemia suspected due to primary bone marrow disease, malignancy, autoimmune disease, GI bleeding, and unknown/unclear cause should be referred to a referral hospital.

FURTHER READING

- Michael J. Cascio, Thomas G. DeLoughery. Anemia Evaluation and Diagnostic Tests. Med Clin N Am - (2016) http://dx.doi.org/10.1016/j.mcna.2016.09.003.
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7.1.2 IRON DEFICIENCY ANEMIA

BRIEF DESCRIPTION

- Iron deficiency anemia is a common cause of anemia worldwide.
- The major causes of iron deficiency anemia are nutritional deficiency, impaired absorption form the GI tract, and chronic blood loss from the GI or genitourinary tract Examples: hook worm infestation, colonic cancer, bleeding peptic ulcer or gastric cancer, prolonged or excessive menstrual bleeding, gynecologic malignancies.

CLINICAL FEATURES

- In addition to the general clinical features anemia (mentioned above), chronic iron deficiency anemia might show unique clinical features.
  - Pica: desire (craving) to eat unusual substances like soil, ice.
  - Koilonychia: Thin, brittle nail with depressed (concave or spoon) distal half.
  - Glossitis or angular stomatitis: the tongue and angel the mouth inflamed and sore.
  - Plumer-vinson syndrome: Difficulty of swallowing due to esophageal webs.
- **Investigations specific for iron deficiency anemia**
  - CBC: low Hg and hematocrit, low MCV, low MCH, and increased RDW.
  - Iron studies
    - Serum Ferritin: usually ow (it could be high in patients with vhronic inflammation or CKD in spite of iron deficiency)
    - Serum iron: may be low or normal
    - Total iron binding capacity (TIBC): usually high
    - Transferrin saturation (TSAT) = serum iron/ TIBC X 100%: low (<20%)

  - Clinical evaluation and investigation to identify the possible cause of bleeding
    - Stool for ova of parasites
    - Digital rectal examination
    - Gynecologic examination
    - Upper GI endoscopy and/or colonoscopy.
- **Pharmacologic treatment of iron deficiency anemia**
  - **Treatment of the underlying cause**
    - The cause of the iron deficiency state should be identified and treated.
    - Oral iron (tablet): For at least three months following correction of the anemia
    - Ferrous sulfate, 325mg (has 65mg elemental iron), PO, TID.

      OR
    - Ferrous fumarate, 324mg, (has 106 elemental iron), PO, BID.

      OR
    - Ferrous gluconate, 325mg P.O. (39mg elemental iron), 1-2tabs, TID
    - Oral iron (solutions/syrup): if the tablets are not tolerated or patient preference
    - Iron hydroxide polymaltose syrup (Each 5ml contains 50mg elemental iron), 10ml PO, BID to TID.

      OR
    - Ferrous gluconate syrup (Each 5ml contains 24mg elemental iron), 15ml, PO TID.

      OR

    - Ferric ammonium citrate syrup (Each 15ml contains 32.8mg elemental iron), give 30ml, TID.

- **How to instruct oral iron intake?**
  - Preferably to be taken 2 hours before or 4 hours after meal.
  - If separating from food is difficult due to gastrointestinal side effects, foods which significantly interfere with iron absorption should be avoided when the iron is given e.g. milk, eggs, tea, and coffee.
  - GI side effects are very common with oral iron administration. These include epigastric pain, nausea or vomiting, constipation or diarrhea, metallic taste.
  - For patients who do not tolerate, they may be advised to take it with meals, or to take a smaller dose, solutions or elixir forms.
- **Intravenous (IV) iron**

Indications for IV iron therapy

  - Intolerance to oral iron therapy.
  - Anemia secondary to chronic kidney disease with a requirement for erythropoietin.
  - No improvement in hemoglobin after 4 weeks of oral iron.
  - Existence of conditions that interfere with absorption of iron from the GI tract e.g., atrophic gastritis, gastrectomy, inflammatory bowel disease
  - Blood loss difficult to cope with oral iron therapy e.g., heavy menstrual bleeding, bleeding telangiectasia
  - Severe anemia during late second or third trimester of pregnancy
- **IV iron administration**
  - For **patients not on hemodialysis:**
    - **Iron sucrose** 200mg, IV, administer over 5 minutes, every 3 days for a total of 5 doses (a total of 1000mg). This dose is usually

sufficient but if hemoglobin is not corrected, additional doses can be given.

OR

  - **Iron sucrose** 200mg diluted in 100ml NS; administer over 30 minutes.

- o **For patients on hemodialysis**
  - **Iron sucrose** 100mg, IV, over 2-5 minutes, given early during dialysis sessions (within the first hour) until iron deficiency is corrected. It needs to be given again, if iron deficiency persists or recurs.

REFERRAL

- Patients with iron deficiency anemia due to GI bleeding or unknown cause or those with known reversible cause but refractory to iron therapy should be referred to a referral hospital.

FURTHER READING

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7.1.3 MEGALOBLASTIC ANEMIA

BRIEF DESCRIPTION

- Megaloblastic anemia is a morphologic term that describes abnormal red blood cells with maturation defects; the red blood cells tend to be large.
- The major causes of megaloblastic anemia are vitamin B12 (Cobalamin) and folate deficiency or a combination of both,
- The pathologic process which results in megaloblastic anemia can also result in leukopenia and thrombocytopenia. In case of Vitamin B12

deficiency the nervous system can be affected.

- Major causes of vitamin B12 deficiency
    - Gastric **origin (pernicious anemia, chronic atrophic gastritis)**
    - **Small intestine malabsorption (chronic diarrhea from small bowel/ileal pathologies)**
    - Strict vegetarians.
- Major causes of folate deficiency
    - Poor nutritional status
    - Increased demand during pregnancy and lactation
    - Alcoholism
    - Drugs: anti-epileptic drugs (phenytoin, phenobarbitone) or drugs which affect Folate metabolism (Methotrexate, cotrimoxazole)
    - Malabsorption
    - Critical illness

CLINICAL FEATURES

- In addition to the clinical features of anemia due to any other cause, some clinical manifestations may suggest megaloblastic anemia.
    - Gossitis (pain over the tongue with smooth, beefy red tongue)
    - Angular
    - Jaundice
    - Neurologic or neuropsychiatric manifestation: specific to vitamin B12 deficiency, but not folate deficiency
    - Neuropathic pain in the lower limbs
    - Decreased position sensation and gait disturbance
    - Weakness of the lower extremities

- Irritability, depression, disorientation, dementia, frank psychosis

DIAGNOSIS AND INVESTIGATIONS

- Investigations for megaloblastic anemia
  - CBC
  - Anemia with high MCV (>100fl). When there is concomitant iron deficiency, the MCV can be normal or low.
  - Leukopenia and thrombocytopenia may also be found.
  - Peripheral morphology: hypersegmentation of neutrophils, large RBCs (macro-ovalocytes).
  - Hypersegmentation of neutrophils is defined as >5% of neutrophils with 5 or more lobes.
  - Bilirubin: Indirect hyperbilirubinemia
  - Determination of the levels of vitamin B12 and Folate
  - Serum vitamin B12 level
  - Serum folate level
  - RBC folate level: to be requested if serum folate level is normal
  - Bone marrow aspiration: indications
  - If the serum vitamin B12 and folate levels are normal but there is strong clinical suspicion.
  - When there is need to exclude other causes.
  - Determining the cause of the deficiency: if the cause is not clinically obvious, further wok up will be needed to identify the underlying cause.

TREATMENT

- **Objectives of treatment**
  - Improve functional status of the patient by correcting the anemia
  - Correct existing and prevent further neuropsychiatric manifestations

  - Identify and treat the underlying cause
- **Pharmacologic treatment of vitamin B12 (Cobalamin) deficiency**
  - **Cyanocobalamin (Vitamin B12)** 1000micrograms (1mg), IM, to be given according to the following schedule
    - Every day for one week
    - Every week for four weeks. If hemoglobin has not normalized, continue weekly until it gets normal.
    - If the underlying disorder persists, 1mg every month for the rest of the patient's life.
- **Pharmacologic treatment of folate deficiency**
  - **Folic acid**, 1 to 5mg P.O., daily for 1-4 months, or until complete hematologic recovery.
  - **Vitamin** B12 level should be checked before giving folic acid alone; as treatment with folic acid alone might worsen neurologic manifestation of vitamin B12 deficiency.
  - If vitamin B12 can't be checked, both Folic acid and vitamin B12 should be started at the same time.
- **Follow up of treatment response**
  - Symptomatic improvement
  - Hemoglobin level

REFERRAL

- Refer patients to a hospital with hematology and gastroenterology services
  - If the underlying cause is not clinically obvious.
  - If other causes of anemia/cytopenia cannot be excluded.
  - Lack of response to the treatment provided.

FURTHER READING

1. Ralph Green, Ananya Datta Mitra. Megaloblastic Anemias Nutritional and Other Causes. Med Clin N Am - (2016) -http://dx.doi.org/10.1016/j.mcna.2016.09.013. medical.theclinics.com
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7.1.4 ERYTHROCYTOSIS (POLYCYTHEMIA)

BRIEF DESCRIPTION

- Erythrocytosis, also called polycythemia, refers to abnormally increased red blood cell count as measured by hematocrit, hemoglobin or RBC count above the sex-specific normal range.
- The following terminologies are important
  - **Relative versus absolute erythrocytosis**
    - **Relative erythrocytosis** is a clinical situation in which there is a decrease in plasma volume resulting in apparent erythrocytosis. It is the result volume contraction, not an increase in RBC count.
    - **Absolute erythrocytosis** indicates a true increase in the RBC mass.
  - **Primary versus secondary erythrocytosis:** Absolute erythrocytosis can be primary or secondary.
    - **Prim**ary erythrocytosis is an autonomous production of RBCs by the bone marrow without any physiologic stimuli. The most important cause of primary erythrocytosis is polycythemia vera (PV).
    - Secondary erythrocytosis results pathologies which increase serum erythropoietin level and stimulate RBC production (see the table below).

- Polycythemia Vera (PV) is a myeloproliferative neoplasm characterized by high RBC count, increased risk of thrombosis and vasomotor symptoms. A gain-of-function mutation in Janus kinase 2 (JAK2) is found in about 98% of patients with PV
- Distinguishing Polycythemia Vera (PV) from secondary erythrocytosis is very crucial.

Table 7.1: Major causes of secondary erythrocytosis

Mechanism	**Major causes**
Hypoxia driven	Chronic lung diseases e.g., COPD, fibrotic lung diseases
	Obstructive sleep apnea
	Smoking
	Long term carbon monoxide exposure
	Cyanotic congenital heart diseases
Renal causes (renal hypoxia driven)	Renal cysts
	Hydronephrosis
	Renal artery stenosis
Paraneoplastic erythropoietin secretion	Renal cell carcinoma
	Hepatocellular carcinoma
	Uterine myoma
Miscellaneous	Post kidney transplant erythrocytosis
	Drug induced erythrocytosis: Erythropoietin, testosterone

CLINICAL FEATURES

- **Asymptomatic:** erythrocytosis is mainly a laboratory finding, the patient could be asymptomatic.
- **Symptomatic**: the symptoms and signs in patients with erythrocytosis can originate from the following reasons.
  - Due to increased blood viscosity (high RBC mass)

  - Due to the underlying cause in secondary erythrocytosis
  - Symptoms and signs specifically related to polycythemia vera
- Clinical features due to the increased viscosity of blood
  - Myalgia, fatigue, headache
  - Blurred vision or transient loss of vision, decreased cognition.
  - Paresthesia
  - Chest discomfort, abdominal pain
- Symptoms and signs suggestive polycythemia vera (PV)
  - Pruritus after bathing
  - History of arterial or venous thrombosis (e.g., ischemic stroke) or venous thrombosis (e.g., DVT, PE, hepatic vein thrombosis)
  - Erythromelalgia (episodic or persistent, intense pain over the toes or fingers with erythema or hotness)
  - Splenomegaly.
- Clinical features that suggest specific secondary causes
  - Symptoms of chronic lung diseases: cough chest tightness, wheezing, and shortness of breath.
  - Symptoms suggestive of obstructive sleep apnea: day time sleepiness, fatigue, apneic (breathless) spells at night, and snoring.
  - History of smoking or long-term exposure to carbon monoxide (indoor smoke).
  - Clinical evidence of neoplasm for paraneoplastic causes: e.g., hepatocellular carcinoma, renal cell carcinoma

DIAGNOSIS AND INVESTIGATION

Investigations

Investigations useful to identify possible causes

- CBC
  - Thrombocytosis and/or leukocytosis: suggestive of PV
  - Erythrocytosis with low MCV: suggestive of PV
- Chest X-ray: if the history and physical examination suggest underlying lung disease.
- Abdominal ultrasound: to look for liver mass, renal cysts or solid mass.
- **Serum erythropoietin (EPO) level**
  - When there are no obvious secondary causes, determination of the serum EPO level helps to differentiate primary from secondary causes.
    - Elevated EPO = secondary causes
    - Low or normal EPO = primary cause, mainly PV.
- **Testing for the JAK2 (Janus kinase 2) mutation**
  - It is essential to test for JAK2 mutation when PV is considered.
  - This test should only be ordered by a specialist who would treat and follow these patients i.e., a hematologist or an internist who follows these patients.
  - 95 – 100% of patients with PV have a JAK2 mutation involving either exon 14 or 12.
- **Bone marrow biopsy**
  - May be needed if secondary cause is not apparent and JAK2 cannot be done.

DIAGNOSIS

- Erythrocytosis is said to be present in adults when one or more of the followings is present:
  - Hematocrit >48% in women or >49 %in men.
  - Hemoglobin: >16.0 g/dL in women or >16.5 g/dL in men.

TREATMENT

OBJECTIVES OF TREATMENT

- Treating the underlying cause
- Decrease symptoms related to hyper viscosity
- Decrease the risk of thrombosis

TREATMENT OF SECONDARY ERYTHROCYTOSIS

- **Treat the underlying cause: Examples**
    - Stop smoking,
    - Decrease/avoid indoor carbon monoxide exposure
    - Treatment of the underlying lung disease e
    - Surgery for renal cell carcinoma.
- **Limited phlebotomy for secondary erythrocytosis**
    - Limited phlebotomy is appropriate in secondary erythrocytosis, if there are symptoms of hyper viscosity (headache, slow mental function, transient loss of vision, paresthesias) and hematocrit is usually > 65%.

TREATMENT OF POLYCYTHEMIA VERA

- **Risk stratification**:patients with either of the following two characteristics are considered high risk
    - History of arterial or venous thrombosis, irrespective of age.
        - Age >60 years are considered high risk. The rest are considered low risk.
- **Phlebotomy (Therapeutic phlebotomy)**
    - For all patients with PV (both low and high risk)
    - Target hematocrit is < 45%
    - One to two units per week until target is achieved. For those who do not tolerate (elderly, women, cardiac or pulmonary disease) reduce to half to one unit per week.

- **Aspirin**
    - **For all patients with PV**
        - **Aspirin** 75-100mg, PO, day.
- **Cytoreductive therapy**
    - To be decided by a specialist.

REFERRAL

- All patients suspected of polycythemia vera should be referred to hematologist for diagnosis and management.

FURTHER READING

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7.2 THROMBOCYTOPENIA

7.2.1 THROMBOCYTOPENIA IN HOSPITALIZED PATIENTS

Brief description

- Thrombocytopenia is defined as a platelet count less than 150 × 10^3 per μl.
- The degree of thrombocytopenia can be divided from mild to severe. However, these numbers should be interpreted cautiously as severity

definitions may vary.

- Mild = 100,000 to 150,000/ µl
- Moderate = 50,000 to 99,000/ µl
- Severe <50,000/ µl

- The safest platelet count at which bleeding is unlikely to occur is not precisely known. It also varies significantly with the underlying cause.
  - Surgical bleeding risk is high when platelet counts <50,000/ µl. (<100,000/ µl for neurosurgery or major cardiac or orthopedic surgery).
  - Severe spontaneous bleeding: the risk is high when platelet counts <20,000 - 30,000/ µl
- Thrombocytopenia is not only a risk for bleeding but it can also be a manifestation of life-threatening thrombotic disorders.
  - Common clinical disorders which can cause thrombosis and thrombocytopenia at same time
    - DIC (disseminated intravascular coagulation)
    - HIT (Heparin induced thrombocytopenia)
    - TTP/HUS (thrombotic thrombocytopenic purpura/hemolytic uremic syndrome
    - APS (antiphospholipid antibody syndrome)
- Thrombocytopenia is a common in hospitalized patients. The risk is even much higher in critically ill patients.
- The causes of thrombocytopenia in hospitalized patients are numerous causing diagnostic challenges. Some of them are listed in the table below.

Table 7.2: ***The major causes thrombocytopenia in hospitalized patients***

1. Spurious thrombocytopenia (Pseudo thrombocytopenia)
2. Hemodilution: massive transfusion or crystalloid resuscitation
3. Sepsis
4. Malaria
5. Disseminated intravascular coagulation (DIC)
6. Heparin induced thrombocytopenia (HIT)
7. Drug induced thrombocytopenia
8. Pregnancy complications: gestational thrombocytopenia, preeclampsia, HELLP syndrome, acute fatty liver of pregnancy, DIC
9. Chronic liver disease and hypersplenism.
10. Alcohol or nutritional deficiencies (Vitamin B12 and/or folate deficiency)
11. Thrombotic microangiopathies (TMA): TTP/HUS (Thrombotic thrombocytopenic purpura/Hemolytic uremic syndrome), catastrophic APS
12. Autoimmune (Rheumatologic) diseases: SLE
13. Post transfusion purpura
14. Viral infections: HIV, Hepatitis C

CLINICAL EVALUATION OF THROMBOCYTOPENIA IN ACUTELY ILL HOSPITALIZED PATIENTS

- Confirmation of the thrombocytopenia:
    - Platelet clumping is a laboratory artifact than cause spurious thrombocytopenia.
    - Repeat CBC

  - Using EDTA-free tubes (e.g. heparin or citrate tubes)
  - Do peripheral morphology to see if the thrombocytopenia is genuine or not.
- Detailed clinical history and physical examination: Evaluate if the underlying disease (e.g., sepsis) is a possible cause
- Evaluating for life threatening causes
  - Sever malarias peripheral blood smear (thin and thick)
  - HIT: History of heparin administration, date of administration, the presence of thrombosis, the degree of decrease in platelet count from baseline in percentage.
  - TTP/HUS: Peripheral morphology for fragmented RBCS, serum LDH, BUN and serum creatinine, urinalysis
  - Acute leukemia: other cell line, peripheral smear and bone marrow aspiration
  - DIC: determine PT(INR) and PTT, peripheral smear
  - Transfusion history: transfusion associated pupura
- Detailed drug history
- Evaluate for other common causes
  - Liver disease: clinical evaluation and liver function tests
  - Viral causes: HIV and HCV screening
  - Alcohol intake
  - Nutritional status: Peripheral blood smear to see evidence of megaloblastic anemia.

TREATMENT

- Treatment of the underlying cause: is the main stay of management in acutely ill hospitalized patients with thrombocytopenia.
- Platelet transfusion: Indications

  - **Active bleeding:** If there is active bleeding and the platelet count <50,000cells/µl.
  - **Prophylactic platelet transfusion**: In patients without active bleeding prophylactic platelet transfusion should be avoided unless the platelets count < 10,000 cells/µl.
- Hold antiplatelet agents and anticoagulants, if platelets count < 30,000cells/µl.

REFERRAL

- Patients in whom the cause of thrombocytopenia is not identified.
- Patients in whom the cause of thrombocytopenia is identified but treatment cannot be provided in that setting.

FURTHER READING

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2. Andreas Greinacher and Sixten Selleng. How I evaluate and treat thrombocytopenia in the intensive care unit patient. Blood. 2016;128(26):3032-3042.
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_7.2.2 IMMUNE THROMBOCYTOPENIA (ITP)

BRIEF DESCRIPTION

- Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by a low platelet count resulting from platelet destruction
- Other conditions which can cause immune related thrombocytopenia should be excluded before the diagnosis ITP. E.g., HIV, HCV infection, H. Pylori infection, systemic lupus erythematosus, chronic lymphocytic

leukemia should be excluded before the diagnosis of ITP. Hence, ITP is a diagnosis of exclusion.

- Patients with other associated conditions (e.g., other autoimmune diseases) are described as having secondary immune thrombocytopenia.
- The incidence of ITP is higher in children than adults. Preceding viral infections are common precipitants of ITP in children.
- Classification of ITP based on the duration of the disease
    - o Newly diagnosed ITP: ITP duration of less than 3 months
    - o Persistent ITP: ITP duration of 3-12 months
    - o Chronic ITP: ITP duration of more than12 months

CLINICAL FEATURES

- Asymptomatic:The vast majority of patients with ITP are not symptomatic, unless the platelet is very low.
- Bleeding mucocutaneous bleeding also called "Platelet-type" bleeding)
    - o Petechiae, purpura, and easy brusing.
    - o Epistaxis, gingival bleeding, menorrhagia, gross hematuria
    - o Gastrointestinal bleeding: bloody vomitus, bleeding peer rectum
    - o Intracranial bleeding: headache, change in mental status or focal neurologic deficit
    - o Signs of anemia: Pallor, tachycardia, low blood pressure or postural drop in blood pressure (if massive bleeding)

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of ITP is made based on clinical grounds after exclusion of other causes of thrombocytopenia.
- A platelet count of < 100,000/µl is needed for consideration of the diagnosis.
- Peripheral blood smear: is required to exclude other causes of

thrombocytopenia and to confirm the presence of true thrombocytopenia.

- Serologies: HIV and HCV (hepatitis C Virus) serology tests are needed in all patients
- H. Pyolri test: is indicated in all patients.
- ANA might be needed is there is a clinical evidence of SLE.
- TSH: autoimmune thyroid diseases are common in patients with ITP.
- Bone marrow aspiration/biopsy:
  - It is not generally indicated for the diagnosis of ITP
  - It is indicated in individuals with atypical features such as B-symptoms, lymphadenopathy, splenomegaly, unexplained leukocyte abnormalities or unexplained anemia, and age > 60 years.
  - It is also indicated before splenectomy.

TREATMENT

OBJECTIVES OF TREATMENT

- Increase the platelet count to a safe level to prevent major bleeding. Safe level of platelet is >30,000/μl.

N.B.:The aim of ITP treatment is not to bring the platelet to normal levels

NON PHARMACOLOGIC

- **Emergency platelet transfusion**
  - Generally, platelet transfusion should be avoided.
  - Indication for platelet transfusion: life-threatening bleeding only.
  - If platelet transfusion is indicated, intravenous steroids should be started immediately.
- **Splenectomy:** is an option of treatment for patients who have corticosteroid refractory or dependent disease.

PHARMACOLOGIC

- Not all patients with ITP need treatment. Those with no indications to treatment should be followed with CBC and clinical assessment of bleeding. The patients should be given enough information about bleeding.

- Indications for tr**eatment**
  - Platelet count < 30,000/μl, irrespective of bleeding status.
  - Platelet count > 30,000/μl and significant bleeding (other than minor mucocutaneous bleeding)
- **First line: Corticosteroids**
  - **Dexamethasone,** 40mg, oral or IV, daily for 04 consecutive days with no tapering. Repeat this 4 day cycles every 2-4 weeks for 4-6 cycles.

    OR
  - **Prednisolone,** 1mg/kg for 1-2 weeks, if there is response taper over a period of six weeks or less.
    - Typical tapering regimen: After response, reduce by 10 mg/week until 0.5 mg/kg is reached; then taper by 5mg/week.
- **Treatment response**
  - Response: is defined if there is a platelet count >30,000/μl and at least doubling from the baseline both must be fulfilled.
  - Durable response: if there is response persisting up to 6 months.
  - Remissio**n:** is defined if platelet count is >100,000//μl for >12 months
- **Steroid dependent:** Ongoing need for continuous prednisolone > 5 mg/d (or equivalent) or frequent courses of corticosteroids needed to keep a platelet count >30,000/μl.

ALTERNATIVE TREATMENTS:

- Intravenous immunoglobulin (IVIg)
- Anti-D
- Rituximab
- Splenectomy

Note: alternative treatments are indicated for steroid resistance or dependent, special population with specific indications and these treatments should only be provided by hematologist or specialist who has experience in using these agents.

REFERRAL

- Patients with suspected secondary causes, atypical presentation (see above), steroid dependent /resistant ITP should be referred to a referral hospital with hematology service.

FURTHER READING

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7.3 BLOOD TRANSFUSION AND TRANSFUSION REACTIONS

- Blood and blood products are scare and transfusion is associated many adverse effects which range from mild to fatal.
- Use blood and blood products when they are appropriately indicated; use when there are no other means to effectively manage the patient's need.
- Blood products should be prescribed n ot only based on cut-of laboratory values (hemoglobin, platelet) but also depending on according individual's clinical status
- Do not use blood transfusion for enhancing wound healing, to improve the general well-being of the patient or just to be on the safe side before surgery.

Characteristics of blood products commonly used in primary care setting

- **Whole Blood**
    - Contains red cells, plasma, stable coagulation factors (VII, XI), and others
    - It does not have functional platelets and labile coagulation factors (V and VIII)
    - 1 unit is about 450 ml of blood; obtained from a single donor
    - Indication
        - Acute blood loss with hypovolemia
        - For anemia when packed RBC (RBC concentrate is not available
    - Caution during whole blood transfusion
        - Start the transfusion within 30 minutes of removal from the refrigerator, and completed within 4 hours of starting
        - Should not be warmed unless indicated (warming by putting on the patient's or other individual's body is not necessary)
- **Packed red cells (Red Cell Concentrate)**
    - Contains red blood cells with little to no plasma, fewer leucocytes, and no citrate.
    - It is indicated in patients with anemia, not due to acute ongoing bleeding.
    - Provide in patients with symptomatic anemia with hemoglobin <8g/dL
    - Transfusion must be started within 30 minutes of removal from the refrigerator, and completed within 4 hours of starting.

ADVERSE REACTIONS TO TRANSFUSION

- Different types of reactions can occur during or after transfusion
    - **Acute reaction**

    - Intravascular hemolysis (ABO incompatibility): severe and life threatening
    - Anaphylactic reaction
    - Transfusion associated circulatory overload (TACO)
    - Bacterial contamination
    - Allergic (mild, mucocutaneous)
    - Febrile, non-hemolytic transfusion reaction
  - **Delayed reaction**
    - Coagulation abnormalities from large volume transfusion
    - Transfusion-transmitted infections
- **Principles of management in acute reactions**
  - The patient should be observed for the first 10 minutes after a new transfusion is started, and vital signs recorded
  - Always store blood used for the compatibility testing at 2-8 degree Celsius
  - Stop the transfusion, and remove the giving set.
  - Check the blood pack labels and patient's identity.
  - Inform the blood bank
  - Re-grouping and testing
  - In mild reactions give antihistamines
  - In moderate to severe reaction provide normal saline infusion +/- adrenaline.

FURTHER READING

1. D B L McClelland. Handbook of Transfusion Medicine. United Kingdom Blood Services 4th Edition. ISBN-10 0 11 322677 2

2. Practice Guidelines for Blood Transfusion: A Compilation from Recent Peer Reviewed Literature Second Edition. American Red Cross 2007. http://www.aabb.org

3. The clinical use of blood. World Health Organization Blood Transfusion Safety 2002.

7.4 VENOUS THROMBOEMBOLIC DISEASE (VTE)

7.4.1 VENOUS THROMBOEMBOLIC DISEASE (VTE) PROPHYLAXIS

- Venous thromboembolic disease (VTE) refers thrombosis (clot) that occurs in the deep veins, called deep vein thrombosis (DVT), or embolization in to pulmonary arterial circulation called pulmonary embolism (PE).
- VTE is a major cause of death and mortality among patients admitted for both surgery and acute medical care.
- The major risk factors that predispose patients for the development of VTE are well known.
- Provision of prophylaxis for hospitalized patients who are at high risk of VTE is an established strategy which decreases death and morbidity.
- The major risk of pharmacologic prophylaxis with anticoagulants or antiplatelets is increased risk of bleeding; hence, the risk of bleeding should also be assessed along with assessment for the risk of VTE.

VTE PROPHYLAXIS IN SURGICAL PATIENTS

- Risk assessment for VTE in surgical patients mainly depends on the type of surgery and the bleeding risk associated with the procedure.

Table 7.3: The indications for VTE prophylaxis in surgical patients

Type of surgery	**Need for pharmacologic VTE prophylaxis**	**Recommended thromboprophylaxis**	**Duration**
Major orthopedic surgery	Yes	First line • Enoxaparin 40mg, sc, daily Or • Rivaroxaban 10mg, po/day Second line • Unfractionated heparin 5,000 IU SC, BID	2-4 weeks Starting 12 hours after surgery
Major general surgery	Yes	Enoxaparin (same dose as above) Or Unfractionated heparin (same dose as above)	2-4 weeks
Major neurosurgery	No		
Laparoscopic cholecystectomy	No		
Transurethral prostatectomy or radical prostatectomy	No		
Cardiac or vascular surgery	yes	Enoxaparin (same dose as above) Or Unfractionated heparin (same dose as above)	

Major trauma	Yes	Enoxaparin (same dose as above) Or Unfractionated heparin (same dose as above	
Major gynecologic	Yes	Enoxaparin (same dose as above) Or Unfractionated heparin (same dose as above	

VTE PROPHYLAXIS IN MEDICAL PATIENTS

- The major risk factors for VTE among medical patients hospitalized for acute care
    - ICU admission (critical care),
    - Stroke with lower limb paralysis
    - Active cancer
    - Known thrombophilia (inherited or acquired)
    - Prolonged immobilization ≥ 3days
    - Heart failure
    - Acute respiratory failure
    - Sepsis
    - Chronic inflammatory diseases
- The presence of one or more risk factors puts the patient at increased risk.
- The higher the number of the risk factors, the higher the risk of developing VTE.
- Although not widely validated, there are a few risk assessment models

designed to help clinicians make a better risk assessment and decide on the provision of prophylaxis.

- We the use of one of the risk assessment tools: IMPROVE-VTE risk assessment model (see the table below).
- Before starting prophylactic anticoagulation assessment of the risk of bleeding is as important as assessing the risk of VTE. Use the IMPROVE-VTE bleeding risk assessment tool given below.
- The major contraindications for pharmacologic prophylaxis
  - Active bleeding
  - Intracranial hemorrhage of any cause
  - Thrombocytopenia (<50,000 or <100,000 with additional risk factor)
  - Major surgery planned in the coming 12 hours.
- If a patient has a high risk of bleeding based on clinical evaluation or using the improve VTE bleeding risk assessment, prophylactic anticoagulation should be avoided.
- Options for pharmacologic prophylaxis
  - Enoxaparin 40mg, SC, daily for the time of hospitalization during acute illness

    OR

  - Unfractionated heparin 5,000 IU, SC, BID for the time of hospitalization during acute illness 3 - 4 weeks

Table 7.4: Improve VTE risk assessment model

No.	Risk factors at admission	Points
	Known thrombophilia	3
	Previous VTE	3
	Malignancy (Active or treated in the last 6 months)	1
	Current lower limb paralysis	2

	Immobility ≥ 7 days	1
	Age >60 years	1
	ICU stay	1

- Score 0-1 = low risk, no need for prophylaxis
- Score 2 -3 = moderate risk, needs prophylaxis
- Score > 4 = High risk, needs prophylaxis

Any score 2 or above = Needs for prophylaxis

Table 7.5: Improve VTE Bleeding risk assessment

No.	**Risk factor**	**Score**
	Active GI bleeding	4.5
	Bleeding in the past three months before admission	4
	Platelet count <50,000	4
	Age ≥ 85	3.5
	Hepatic failure (INR>1.5)	2.5
	Severe Renal Failure (GFR <30ml/min)	2.5
	Liver failure (INR>1.5)	2.5
	Any ICU admission	2.5
	Central venous catheter	2
	Rheumatic disease	2
	Active cancer	2
	Age 40-84	1
	Male	1
	Moderate renal failure (GFR 30-59ml/min)	1

A score >7 is considered high risk for bleeding

FURTHER READING

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2. D. R. Anderson, G. P. Morgano, C. Bennett, F. Dentali et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. Blood advances 10 Dec 2019. Volume 3, Number 23.

7.4.2 VENOUS THROMBOEMBOLISM (VTE) DISEASE: DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

BRIEF DESCRIPTION

- Venous thromboembolism (VTE) is a condition in which blood clot (thrombus) forms in a vein.
- One of the common sites for thrombus formation in the deep veins of the legs or pelvis. This is known as deep vein thrombosis, or DVT.
- The thrombus can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as pulmonary embolism, or PE.
- The term 'VTE' includes both DVT and PE.
- Venous thromboembolic disease covers a spectrum ranging from asymptomatic calf vein thrombosis to symptomatic DVT or PE.
- Pulmonary embolism can fatal, if it is not detected and treated early.
- Non-fatal VTE can cause serious long-term complications

Risk factors for VTE

- Immobility
- Previous VTE
- Major surgery, e.g., orthopedic, abdominal and pelvic surgery
- Trauma especially involving the pelvis and lower limbs
- Pregnancy and postpartum state
- Contraceptive pill use, hormone replacement therapy (HRT)
- Cancer
- Medical conditions, e.g., Heart Failure, nephrotic syndrome, SLE, IBD
- Inherited disorders causing hypercoagulability

CLINICAL FEATURES

Symptoms

- Swelling calf or thigh (usually unilateral)
- Pain in the affected limb
- Breathlessness (may be intermittent)
- Sharp chest pain, cough
- Blood-stained sputum
- Dizziness, fainting or collapse

Signs

- Occasionally tenderness in the limb
- Tachypnea /tachycardia/low oxygen saturation
- Hypotension
- Signs of pleural effusion

INVESTIGATIONS AND DIAGNOSIS

- CBC, Chest X-ray, ECG
- Doppler ultrasound of leg and pelvic veins
- Echocardiography
- APTT, INR /PT as baseline
- CT scan of the chest with contrast (CT pulmonary angiography)

TREATMENT OBJECTIVES

- Prevent further clot formation and embolization
- Relieve symptoms
- Prevent death from PE
- Prevent recurrence of DVT/PE and development of pulmonary hypertension/post phlebitis syndrome

NON PHARMACOLOGIC

- Elastic compression stockings after anticoagulation
- Early ambulation after proper anticoagulation

PHARMACOLOGIC

I. Acute treatment

First line

- **Unfractionated heparin** (UFH) 5000 U, IV, bolus; then 250 U/Kg/dose, BID or 17,500U SC, BID (for an average adult) until two consecutive INR values become therapeutic (2-3)

  OR

- **Enoxaparin** 1mg/kg, SC, BID, until two consecutive INR values become therapeutic (2-3)

PLUS

- **Warfarin** (starting simultaneously with heparin)

Starting dose: 5 mg, P.O., daily with regular dose adjustment and monitoring of INR until target of 2.0-3.0 is attained.

- N.B: Enoxaparin dose should be reduced or it should be avoided in patients with advanced CKD (GFR<30ml/min)

Alternatives

- **Rivaroxaban** 15mg PO BID X 3 weeks
    - Rivaroxaban should be avoided in patients should be avoided in patients with advanced CKD (GFR<30ml/min)

II. Chronic treatment

- **Warfarin**, dose adjusted to achieve target INR of 2.0-3.0

  OR

- **Rivaroxaban** 20mg po, daily.

III. Duration of anticoagulation

- Patients with VTE due to a reversible/time-limited risk factor (e.g., surgery): 3-6 months.
- Patients with first episode of idiopathic/unprovoked VTE: 3-6 months
- Most patients with advanced malignancy should be treated indefinitely or until the cancer resolve
- Patients with recurrent idiopathic/unprovoked VTE: indefinitely

REFERRAL

- The following patients need to be referred to a referral hospital with hematology service
    - Recurrent VTE without identifiable risk factors
    - Single episode pulmonary embolism with no identifiable risk factor
    - Patients with significant bleeding While having therapeutic or sub-therapeutic INR

FURTHER READING

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7.5 HEMATOLOGIC MALIGNANCIES

7.5.1 ACUTE LEUKEMIA

BRIEF DESCRIPTION

- Leukemia is a clonal, neoplastic disorder characterized by proliferation and accumulation of immature and malignantly transformed cells in the bone marrow and peripheral blood.
- Leukemias are common malignancies in both children and adults.
- Leukemias encountered in primary care can be classified in to acute and chronic.
- The two major acute leukemia types are acute lymphoblastic leukemia and acute myelogenous leukemia.
- Acute lymphoblastic leukemia is commoner in children and acute myelogenous leukemia is common in older adults.
- Lack of recognition and the resulting delayed diagnosis can prove to be fatal. Hence, primary care providers should be able recognize leukemias

and refer patients as early as possible.

CLINICAL FEATURES

- Acute leukemias present within a relatively short period of time. The presentations are not specific.
- Some of the clinical presentations are the following:
  - **Anemia**: due to bone marrow failure and/or bleeding
    - Fatigue
    - Shortness of breath on exertion
    - Pallor
  - **Bleeding:** Thrombocytopenia due to bone marrow failure
    - Mucocutaneous bleeding: gum bleeding, epistaxis, cutaneous bleeding, gastrointestinal bleeding and petechiae/purpura, excessive menstrual bleeding
  - **Infections:** Dysfunctional leucocytes and/or bone marrow failure
    - Fever
    - Focuses of infections: cellulitis, perianal abscess, gingival infection, pneumonia, urinary tract infection
  - **Other hematologic findings**
    - Bone pain and sternal tenderness
    - Lymphadenopathy
    - Splenomegaly
    - Hepatomegaly

INVESTIGATIONS AND DIAGNOSIS

Investigations

- CBC

- Peripheral smear: Look for circulating blasts
- Bone aspiration
- Lactate dehydrogenase
- Uric acid
- BUN and creatinine
- Liver enzymes
- Serum electrolytes

DIAGNOSIS

- The diagnosis acute leukemia should be suspected in patients presenting with one or more of the above-mentioned symptoms.
- The compete blood count (CBC) might provide an important clue. Marked leukocytosis or leukopenia with anemia and thrombocytopenia indicate the possibility of acute leukemia. However, the leukocyte count can rarely be normal.
- Establishing the diagnosis of acute leukemia requires evaluation of peripheral smear and bone marrow aspiration/biopsy by a hematologist or pathologist.
- Differentiating the sub-types of acute leukemia might require special studies such immunophenotyping by flow cytometry and cytogenetic studies.

TREATMENT

- Patients with suspected or proven acute leukemia should be referred to specialized referral hospital with hematology oncology service as soon as possible.
- Supportive treatment might be needed while referral is being processed.
- Transfusion: Packed RBC transfusion of severe anemia, platelet transfusion or severe thrombocytopenia

- Treatment of infection/neutropenic fever

REFERRAL

- All patients with suspected acute leukemia should be referred (see above)

FURTHER READING

1. A. S. Davis, A. J. Viera and M. D. Mead. Leukemia: An Overview for Primary Care. Am Fam Physician. 2014;89(9):731-738. www.aafp.org/afp
2. BMJ Best practice overview of leukemia last update 24 Sep 2020. https://bestpractice.bmj.com

7.6 CHRONIC LEUKEMIAS

7.6.1 CHRONIC LYMPHATIC LEUKEMIA (CLL)

BRIEF DESCRIPTION

- Chronic lymphocytic leukemia (CLL) is one of the lymphoproliferative neoplasms characterized by a clonal proliferation of functionally incompetent, mature appearing lymphoid cells.
- Small lymphocytic lymphoma (SLL) is a similar disease with predominate lymph node enlargement.
- CLL and small lymphocytic lymphoma (SLL) are considered part of a spectrum of the same disease. Both are characterized by clonal proliferation of mature B-lymphocytes.
- In SLL, there is more lymph node involvement and less bone marrow and peripheral blood involvement; in CLL, the bone marrow and the peripheral blood are more affected.
- The clinical presentation of CLL or SLL relate to tissue infiltration (lymphadenopathy, organomegaly), peripheral blood cytopenia (anemia,

bleeding, infections), or immune suppression (infections and malignancies) and autoimmune phenomenon (hemolytic anemia).

CLINICAL FEATURES

Symptoms

- Asymptomatic
    - A significant proportion of patients can be asymptomatic and the diagnosis is considered with an incidental finding of significant lymphocytosis (leukocytosis with predominant lymphocytes)
- "B" symptoms
    - Unintentional weight loss (10% or above) in six months or less.
    - Fever >38°C or drenching night sweats for 2 weeks or above without evidence of infection.
- Recurrent infections (pneumonia, UTI) caused by usual bacterial pathogens
- Symptoms of anemia: fatigue, exertional shortness of breath
- Symptoms related to enlarged lymph nodes, splenomegaly or hepatomegaly

Signs

- Lymphadenopathy
- Splenomegaly
- Hepatomegaly
- Pallor

DIAGNOSIS AND INVESTIGATIONS

Investigations

- Complete blood count and differential
    - Asses the absolute lymphocyte count, hemoglobin and platelet count.
- Peripheral blood smear for morphology

  - Mature appearing small lymphocytes with smudge (smear) cells
- LDH, Uric acid, liver enzymes, BUN and Creatinine
- Retic count and Coomb's test when autoimmune hemolysis is suspected
- Bone marrow aspiration: is not always needed. It is indicated if there is unexplained cytopenia.
- Lymph node biopsy: it is not routinely needed. It is indicated if there is progressive disease or transformation to aggressive lymphoma is suspected.
- Chest X-ray and abdominal ultrasound: If clinically indicated.

DIAGNOSIS

- The diagnosis of CLL should be strongly considered in patients with absolute lymphocyte count above 5000/ μL. However, confirmation requires review of peripheral blood smear morphology by hematologist or pathologist.
- Definitive diagnosis of CLL requires the presence of the following three parameters.
  - Absolute lymphocytosis defined as lymphocyte count more than 5000 cells/μl.
  - Confirming the presence of excess mature appearing lymphocytes on the peripheral blood smear.
  - Immunophenotyping (Flow cytometry) from peripheral blood: to confirm the presence B-cell markers on the neoplastic lymphoid cells and their clonality.

Table 7.6: Staging of chronic lymphocytic leukemia

Staging			
Rai stage	**Risk**	**Features**	**Overall survival in years**
0	Low	Lymphocytosis in the peripheral blood and bone marrow only	>10
I/II	Intermediate	Lymphadenopathy +/- hepatosplenomegaly	7
III/IV	High	Anemia +/- thrombocytopenia	<4
Binet stage			
A	Low	< 3 areas of lymphadenopathy	12
B	Intermediate	>3 areas of lymphadenopathy	7
C	High	Anemia, thrombocytopenia or both	2 – 4

TREATMENT

OBJECTIVES OF TREATMENT

- Improve symptoms
- Improve survival
- Achieve long periods of remission
- The objective of CLL treatment is not cure

TREATMENT OPTIONS

- Treatment should be decided and provided by a hematologist.
  - Wait and watch with no treatment: for asymptomatic patients
  - Combination chemotherapy

  - Targeted therapies
  - Monoclonal antibody therapies
- **Indications for treatment**
  - Symptomatic disease: B-symptoms, bulky lymph node or splenomegaly > 6cm below the left costal margin.
  - Anemia
  - Thrombocytopenia

REFERRAL

- All patients suspected or confirmed to have CLL need to be referred to a referral hospital with hematology service.

FURTHER READING

1. C. Nabhan and S. T. Rosen. Chronic Lymphocytic Leukemia: A Clinical Review. *JAMA*. 2014;312(21):2265-2276.
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7.6.2 CHRONIC MYELOGENOUS LEUKEMIA (CML)

BRIEF DESCRIPTION

- Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm.
- Myeloproliferative neoplasms are a group of disease characterized by dysregulated proliferation of one or more of the myeloid cell series.

- In addition to CML the other diseases classified as myeloproliferative are polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis.
- CML is mainly characterized abnormal proliferation of the granulocyte cell series.
- CML results from a chromosomal abnormality. Two adjacent chromosomes are involved; namely, chromosome number 9 and 22. A portion of chromosome 9 moves to the end of chromosome 22 and a portion of chromosome 22 moves to the end of chromosome 9, a process called translocation. The abnormal chromosome is called the Philadelphia (Ph) chromosome.
- The break on chromosome 9 leads to a mutation of a gene called *"ABL"* (for Herbert Abelson). The break on chromosome 22 involves a gene called *"BCR"* (for breakpoint cluster region). The resulting fusion gene is called the BCR-ABL gene.
- The *BCR-ABL* fusion gene directs the production of an abnormal enzyme called BCR-ABL tyrosine kinase.
- This abnormal enzyme causes the leukemic changes in the bone marrow myeloid precursor cells.
- This enzyme is the primary target of the current treatment of CML.
- CML has three phases:
  - **Chronic phase**: None of the features in the accelerated phase are present.
  - **Accelerated phase:** defined as the presence of one of the following
    - Blast cells constituting 10 to 19% of the cells in the peripheral blood or bone marrow
    - Basophilia > 20% of the cells in the peripheral blood
    - Persistent thrombocytopenia <100,000/µl
    - Persistent thrombocytosis >100,000/µl unresponsive to therapy

    - Increasing spleen size and WBC count unresponsive to therapy
    - Cytogenic clonal evolution
  - **Blast crisis**: defined as the presence of one of the following
    - Blasts ≥ 20% in the peripheral blood or bone marrow
    - Extramedullary blast proliferation, apart from the spleen
    - Large foci or clusters of blasts in the bone marrow biopsy

CLINICAL FEATURES

- **The chronic phase of CML**

Symptoms

  - **Asymptomatic**
    - Patients in chronic phase CML can be asymptomatic.
    - In such cases diagnosis is suspected form incidental finding of markedly raised white cell count with high granulocyte percentage in the differential count.
  - **Symptomatic:** The symptoms are non-specific
    - Fatigue, poor appetite, weight loss
    - Abdominal (left upper quadrant) abdominal fullness, early satiety: due to splenomegaly
    - History of thrombosis or bleeding
    - Priapism

Signs

  - **Splenomegaly:** it is the most common physical finding in CML
  - Pallor

- **Accelerated and blast crisis phase**
  - In accelerated phase patients tend to be more symptomatic. Spleen

size increases, and symptoms of anemia.

- The presentation in blast crisis phase like that of acute leukemia (infection, bleeding, and rapid deterioration in clinical status)

INVESTIGATION AND DIAGNOSIS

Investigations

- CBC: leukocytosis with or without thrombocytosis and mild anemia
- Uric acid: elevated
- LDH: elevated
- Peripheral blood smear
- Bone marrow aspiration

DIAGNOSIS

- **When to suspect CML?**
  - CML should be suspected in patients with elevated white cell count, usually exceeding 30,000/μl, with elevated granulocyte counts (neutrophils, basophils or eosinophils).
  - Other supportive features: splenomegaly and thrombocytosis (increased platelet count)

DIAGNOSIS CONFIRMATION

- The diagnosis of CML requires the following important diagnostic studies
  - Peripheral blood smear
    - It shows increased granulocyte cell lines at all stages of development (mature, intermediately mature and immature).
  - Bone marrow aspiration
    - Hypercellular marrow with increased myeloid to erythroid ratio.
  - Confirmation of the presence of either Philadelphia chromosome or the abnormal fusion gene (BCR-ABL)

  - Cytogenics for Philadelphia chromosome
  - Fluorescence in situ hybridization (FISH) or reverse transcript for BCR-ABL from peripheral blood.

TREATMENT

- Treatment of CML with targeted tyrosine kinas inhibitors is highly effective, safe and available in Ethiopia.
- Tyrosine kinase inhibitors (TKIs): Imatinib mesylate, Nilotinib, Bosutinib, and Ponatinib.
- Imatinib mesylate is used as first line in most patients.
- The treatment is provided in limited centers with hematologic services; hence, patients need to be referred as soon as the diagnosis is suspected.
- The goal of treatment is not only to achieve clinical and hematologic remission but also a complete molecular remission.

REFERRAL

- All patients with suspected CML should be referred to a referral hospital with hematology service.

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7.7 LYMPHOMAS

BRIEF DESCRIPTION

- Lymphomas are neoplastic transformation of the cells of lymphoid tissues. The origins could in nodal sites (lymph nodes) or extra-nodal sites e.g., gastrointestinal, central nervous system.
- The term lymphoma encompasses two major histologic types: Hodgkin's lymphoma and non-Hodgkin lymphoma.
- Hodgkin 's lymphoma is a distinct group of lymphomas with few histologic sub-types. It predominately involves lymph nodes; extra-nodal involvement is not common. It progresses from one lymph node region to other in fairly predictable fashion.
- Non-Hodgkin's lymphoma (NHL) is a broader category which includes a significantly heterogenous lymphoma with variable clinical, histologic, genetic abnormalities, outcome and treatment characteristics.
- The vast majority of NHLS are B-cell in origin.
- Clinically NHL is classified in to Indolent, aggressive or highly aggressive.
- Indolent lymphomas have slow progression but they are not as responsive as aggressive lymphomas for treatment.
- Immunosuppression, viral infection (Epstein- Barr virus, Human herpes virus-8, hepatitis C virus, HIV), H. Pylori infection, and autoimmune diseases are important risk factors for NHL.
- HIV infection with severe immunosuppression is associated with increased incidence of sets of aggressive/highly aggressive lymphomas which are called HIV-associated lymphomas. These include: Primary CNS lymphoma, Primary effusive lymphoma, HIV-associated large B-cell lymphoma, and HIV-associated Burkitt's lymphoma.

CLINICAL FEATURES

Symptoms

- Painless lymph node enlargement (Lymphadenopathy)

  - In indolent lymphomas the lymph node enlargement can be waxing and waning.
  - The spread in NHL tends to be unpredictable, skipping lymph node regions.
  - Compressive symptoms: Shortness of breath, abdominal mass
- B-symptoms
  - Weight loss: > or = 10% weight loss in < 06 months
  - Unexplained fever (>38.5o C) or drenching night sweats.
- Fatigue
- Extra-nodal symptoms
  - GI symptoms: Diarrhea, GI bleeding, early satiety.
  - Testicular enlargement
  - CNS symptoms: Headache, weakness of extremities

Signs

- Enlarged lymph nodes: all lymph node regions need to be examined
- Splenomegaly
- Hepatomegaly
- Abdominal mass
- Pallor

INVESTIGATION AND DIAGNOSIS

Investigations

- Lymph node biopsy
- CBC
- Uric acid
- LDH

- Liver function test, BUN and Creatinine
- Hepatitis B and C virus serologies, HIV screening
- Staging investigations: Chest x-ray, abdominal ultrasound or CT-scan, bone aspiration or biopsy

DIAGNOSIS

- The diagnosis lymphoma needs lymph node biopsy. FNAC (Fine needle aspiration cytology) is not enough.
- Once a diagnosis of lymphoma is made further investigations are needed for staging, prognosis, and for treatment purposes.

WHEN TO SUSPECT LYMPHOMA?

- Patients presenting with any of the following: lymph node enlargement, splenomegaly, B-symptoms, cytopenia. The clinical presentation may resemble infectious disease like tuberculosis

Table 7.7: Ann Arbor staging of lymphoma

Stage	Area of involvement
I	1. Involvement of a single lymph node region or a single lymphoid organ (e.g. spleen, thymus) (I) OR 2. Involvement of non-lymphoid organ(site) without any lymph node involvement (IE)
II	1. Involvement of two or more lymph node regions or lymphoid organ on the same side of diaphragm.(II) OR 2. Involvement of a single non-lymphoid organ(site) with regional lymph node +/- non-regional lymph node on the same side of the diaphragm. (IIE)

III	Multiple lymph node regions or lymphoid organ on both sides of diaphragm with or without non-lymphoid organ (site) involvement. ○ When extra lymphoid organ is involved =IIIE ○ When spleen is involved = IIIS ○ When both are involved = IIIE, S
IV	Any involvement of the liver or bone marrow, lungs (other than direct extension, or cerebrospinal fluid.
Additional characterization	A: No B-symptoms B: B -symptoms E: Involvement of extra lymphoid organ (site) S: Splenic involvement

TREATMENT

- The treatment of lymphomas depends on whether the lymphoma indolent or aggressive, histologic type, stage, comorbidities, performance status and the risks associated with the treatment.
- Aggressive or highly aggressive lymphomas need urgent treatment.
- Chemotherapy is the main stay of treatment. In localized diseases radiotherapy may be used.
- There are various combination chemotherapeutic regimens used for specific types of lymphomas.
- Treatment decision and follow up should be made by hematologist.

REFERRAL

- All patients with suspected or confirmed lymphoma should be referred to a referral hospital which provides hematology services.

FURTHER READING

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CHAPTER 8:

INFECTIOUS DISEASE

8.1 ANTIMICROBIAL PROPHYLAXIS IN SURGERY

- The antimicrobial prophylaxis choice before surgery depends the most probable contaminating flora at the site of surgery, the risk of infection associated with the specific surgery, local susceptibility pattern, and coverage/activity of the antibiotic.
- The most common organisms causing surgical site infections (SSIs):
  - Staphylococcus aureus
  - Coagulase-Negative staphylococcus
  - Gram negative rods: e.g. *Escherichia coli* and Klebsiella species are also common.
- Antibiotic choices (see the tables below for antibiotic choices in specific surgical areas)
  - **First choice: Cefazolin**
    - Cefazolin should be used as the first line for most surgical procedures. I
    - If cefazolin is not available, the hospital has to take action to avail it.
  - **Alternatives/stewardship**
    - Until Cefazolin supply is ensured, the use of other agents like cefuroxime, Ampicillin/Ampicillin sulbactam is reasonable over third generation cephalosporin and other antibiotics, unless indicated in the table below.

- **Alternatives for allergy:**
  - In the presence of sever penicillin allergy, clindamycin might be used.
- Anaerobic coverage with the addition of metronidazole
  - Metronidazole should be added for colorectal procedures, appendectomy, hysterectomy, and urologic procedures entering the gastrointestinal tract.
- **Clean procedures**:
  - Unless, antimicrobial prophylaxis is not recommended for clean procedures.
- **Timing**
  - One hour (preferably 30-45 minutes) prior to incision (usually with induction anesthesia) so that an effective amount of the drug is available during the contaminating period.
  - If used, fluoroquinolones or vancomycin should be administered 60 to 120 minutes prior to incision.
- **Dose/route**:
  - **Route:** All the prophylactic agents must be administered parenterally (IV) (see few exceptional below).
  - Dose: The effective dose should be governed by the patient's weight. Higher than the usual therapeutic dose is recommended for most agents.
- **Re-dosing**:
  - In procedures lasting 3 hour or less: No re-dosing
  - Procedures lasting longer > 3 hours: an additional dose is needed.
- **Postoperative prophylaxis**
  - Postoperative prophylaxis is strongly discouraged except under bioprosthetic insertion in which case 2 or 3 additional

prophylactic doses may be deemed sufficient.

- **Durations**:
  - Single dose or should be discontinued within 24 hours of the initial dose administrations.
- **No on-call**:
  - Any prophylactic agent should not be given early before surgery (on-call) as it often results in less than effective tissue levels at the time of incision.

ANTIMICROBIAL STEWARDSHIP

- In our setup, one of the basic challenges had been the use of broad-spectrum antimicrobials for prophylaxis, primarily due to the poor supply of cefazolin and sometimes due to resistance by the practitioners.
- The drug and therapeutics committee or hospital administration and others concerned should work to ensure the availability of the first line and alternative surgical prophylactic drugs.
- A restrictive policy (automatic stop order) can be planned and communicated to avoid unnecessary and risk practice of prolonged (>24 hours) antimicrobial prophylaxis.
- Use of vancomycin should be limited for patients with a high risk of MRSA colonization. This may include patient with a recent history or risk of MRSA colonization or infection. Otherwise, cefazolin can safely be used even in settings with a high prevalence of MRSA.
- An authorization policy can easily be implemented for the use of vancomycin, third generation cephalosporins and other advanced antimicrobials from a watch or reserve category that were indicated as alternatives in this guideline. The authorization may involve a prescription approval by an infectious disease specialist, or antimicrobial stewardship team in the ward if available or the most senior surgeon or a clinical pharmacist with an infectious disease or stewardship training.

ANTIMICROBIAL PROPHYLAXIS FOR THE DIFFERENT TYPES OF SURGERIES

Table 8.1: Antimicrobials for gastrointestinal surgeries

Type of surgery/procedure	Likely Pathogens	Prophylaxis Regimen	Comments
Gastroduodenal		Cefazolin 2 g x 1	Clean procedures (without entry to lumen) with low-risk patients do not need prophylaxis
Biliary tract	Gram negative enterics	Cefazolin 2 g x 1 OR Cefotetan 2g x 1	Elective, low risk laparoscopic procedures do not need prophylaxis
Small Intestine (non-obstructed)	Coliforms, Gram positive cocci, enterics	Cefazolin 2 g x 1	
Small Intestine (obstructed)	Gram positive cocci, Gram negative enterics, Coliforms, anaerobes	Cefazolin (2g x1) OR Cefotetan (2g x 1) PLUS Metronidazole (500mgx 1)	
Trauma surgery (Penetrating abdominal trauma)	Coliforms and anaerobes (gm positive and negative)	Cefazolin (2g x1) OR Cefotetan (2g x 1) PLUS Metronidazole (500mg x 1)	2nd dose if surgery lasts> 3hrs

Hernia repair	Gram positive cocci	Cefazolin 2 g x 1	
Colorectal or large bowl	Coliforms, enterococci, Bacteroides, Pepto streptococci, Clostridia	Bisacodyl (2 tabs)	2 days before surgery
		Oral Neomycin (500mg) PLUS Oral Erythromycin (500 mg)	1pm, 2pm and 10pm before surgery
		Cefazolin (2g x1) PLUS Metronidazole (500mg x 1)	30-45min before skin incision, 2nd dose if procedure lasts>3hrs
Appendectomy, Acute appendicitis (Non-perforated)	Coliforms, anaerobes	IV Cefazolin (2g x1) PLUS IV Metronidazole (500mg x 1)	*NB: In perforated or gangrenous cases treatment should continue as clinically indicated*

Table 8.2: Antimicrobials for genitourinary surgeries

Type of procedure	Likely Pathogens	Prophylaxis Regimen	Comments
Prostatectomy	Coliforms, enterococci, Pseudomonads	Cefazolin 1 g x 1 OR Ciprofloxacin 400mg x 1	Fluroquinolones should be administered 60 to 120 minutes before surgical incision. Urinary tract procedures often entering the GI tract needed to be addressed based on colorectal procedures above
Cystoscopy with manipulation (e.g., transrectal prostate biopsy) or upper urinary tract instrumentation	Enteric gram-negative bacilli, enterococci	Ciprofloxacin 400mg x 1 OR Cotrimoxazole	
Cystoscopy with no manipulation or upper urinary tract manipulation		No prophylaxis	
Open or laparoscopic procedures (cystectomy, radical prostatectomy, and nephrectomy with no entry to urinary tract)	Staphylococcus species	Cefazolin 2 g x 1	Since they are clean procedures no prophylaxis unless presence of preoperative catheter or prosthetic placement or unknown risk of bacteriuria or UTI.

Table 8.3: Antimicrobials for gynecology and obstetrics surgeries

Type of surgery	**Likely Pathogens**	**Prophylaxis Regimen**	**Comments**
Cesarean section (CS)	Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci	Cefazolin 2 g x 1	Can be given before initial incision or after cord is clamped.
Hysterectomy	Coliforms, enterococci, streptococci, clostridia, Bacteroides	Vaginal: cefazolin 1 g x 1 Abdominal: cefotetan 1 g x 1 or cefazolin 1 g x 1	Metronidazole 1 g IV x 1 is recommended alternative for penicillin allergy. Course should not exceed 24 hours in duration.
Laparoscopy (diagnostic, tubal sterilization, operative except for hysterectomy) and other clean procedures	None	Not recommended	

Table 8.4: Antimicrobials for head and neck surgeries

Type of surgery	Likely Pathogens	Prophylaxis Regimen	Comments
Clean	No	Not recommended	Cefazolin is required for immunocompromised, prosthetic material placement procedures
Periodontal surgery	None	Not routinely recommended	
Minor clean-contaminated *(high degree of difficulty / long duration, place dental implants, bone graft inserted)*	Oral streptococci (aerobic and anaerobic species) are dominant	Ampicillin/Ampicillin sulbactam	Clindamycin is best alternative for penicillin allergy.
Maxillofacial surgery (major clean-contaminated)	*Staphylococcus aureus*, streptococci, oral anaerobes	Cefazolin 2 g IV PLUS Metronidazole 500 mg IV	Repeat intraoperative dose for operations longer than 4 hours
All forms of head and neck cancer resection	*S. aureus*, streptococci oral anaerobes	Cefazolin 2g IV± metronidazole 500mg IV or Clindamycin 600 mg at induction and q8h x 2 more doses	Add gentamicin for clean–contaminated procedures
Open reduction and internal fixation of facial bone fractures	*Staphylococcus aureus*, streptococci, oral anaerobes	Cefazolin 2 g IV PLUS, metronidazole 500 mg IV	Antibiotics should not be continued postoperatively

Table 8.5: Antimicrobials for cardiovascular and non-cardiac vascular surgeries

Type of Operation	Likely Pathogens	Prophylaxis Regimen	Comments
Cardiac surgery	*Staphylococcus spp., streptococcus spp., Corynebacterium*	Cefazolin 1 g every 8 hours x 48 hours	Patients >80 kg should receive 2 g of cefazolin instead; in areas with high prevalence of *S. aureus* resistance, vancomycin should be considered
Thoracic surgery (lobectomy, pneumonectomy, lung resection, thoracotomy)	*Staphylococcus spp., streptococcus spp., Corynebacterium,* enteric G-ve bacilli	Cefazolin 1 g every 8 hours x 48 hours	First-generation cephalosporins are deemed inadequate, and shorter durations of prophylaxis have not been adequately studied.
Vascular surgery			
Arterial, involving prosthesis, abdominal aorta, or groin incision	*Staphylococcus spp., enteric gram-negative bacilli*	Cefazolin 1 g at induction and every 8 hours x 2 more doses	Although complications from infections may be infrequent, graft infections are associated with significant morbidity
Lower extremity amputation for ischemia	*Staphylococcus spp., enteric gram-negative bacilli, clostridia*	Cefazolin	Clindamycin is an alternative.
percutaneous procedures in adults (Endograft placement)	*Staphylococcus aureus, S. epidermidis*	Cefazolin	Clindamycin is an alternative.

Table 8.6: Antimicrobials for orthopedic surgeries

Type of Operation	Likely Pathogens	Prophylaxis Regimen	Comments
Clean orthopedic procedures	*None*	-	
Joint replacement Spinal procedures Hip fracture repair Internal fixation	*S. aureus, S. epidermidis*	Cefazolin 1-2g x 1 preoperatively, then every 8 hours x 2 more doses	Clindamycin is an alternative. Vancomycin reserved for penicillin-allergic patients or where risk of MRSA warrants use
Open/compound fractures (Gustilo-Anderson fracture type I or II)	*S. aureus, S. epidermidis,*	Cefazolin 1 g x 1 preoperatively, then every 8 hours for a course of presumed infection	Gram positive coverage is reasonable. Antibiotics may be discontinued 24 hours after wound closure.
Open/compound fractures (Gustilo-Anderson fracture type III)	Staphylococcus species and gram-negative bacilli	Cefazolin OR Ceftriaxone + gentamycin	Gram positive and gram-negative coverage needed. Discontinue antibiotic after 72 hours or within a day after soft tissue injuries have been closed.

Table 8.7: Antimicrobials for neurosurgery

Type of Operation	**Likely Pathogens**	**Prophylaxis Regimen**	**Comments**
CSF shunt procedures	*Staphylococcus species*	Cefazolin 1 g every 8 h x 3 doses OR Ceftriaxone 2 g x 1	No agents have been shown to be better than cefazolin in RCTs
Spinal surgery	*Staphylococcus species*	Cefazolin 1-2g x 1	Limited number of clinical trials comparing different treatment regimens
Craniotomy	*Staphylococcus species*	Cefazolin 1-2g x 1 OR Cefotaxime 1-2 g x 1	Trimethoprim-sulfamethoxazole (160/800 mg) IV x 1 can be substituted for patients with penicillin allergy

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8.2 PRINCIPLES OF ANTIMICROBIAL REGIMEN SELECTION

- Antimicrobials are among the widely and often inappropriately used drugs globally.
- Some of the basic principle that has to be applied when prescribing antimicrobial therapy include the following
    - Having accurate infectious diagnosis
    - Knowing the difference between empiric and definitive treatments
    - Pinpointing occasions to shift to narrow-spectrum
    - Cost-effective oral alternatives for the shortest duration required
    - Knowing characteristics that are peculiar to antimicrobials (such as pharmacodynamics and efficacy at the site of infection)
    - Recognizing host characteristics that impact antimicrobial activity; and in turn, identifying the adverse effects of antimicrobials on the host.
    - Understand the importance of antimicrobial stewardship, to discern when to consult infectious disease specialists, and to identify circumstances when antimicrobial therapy is not needed.

- By ensuring these universal principles, all practitioners should be able to use antimicrobials in a responsible way that benefits both the single patient and the community.

DETERMINING APPROPRIATE ANTIMICROBIAL INDICATIONS

- **Accurate Diagnosis:**
    - An accurate diagnosis is the first important step of rational antimicrobial use. This is determined by:
        - Site of infection
        - Defining the host (e.g., immunocompromised, diabetic, of advanced age)
        - Establish microbiological diagnosis (particularly in serious, life-threatening infections, and situations that require prolonged treatment e.g., infective endocarditis, septic arthritis, meningitis).
        - Appropriate specimen collection and prompt submission to the microbiology laboratory, preferably carried before the institution of antimicrobial therapy.
        - Clinical presentation and additional investigations can help to determine the etiologic agent or exclude noninfectious diagnoses.
- **Timing of initial antimicrobial:**
    - In most circumstances, antimicrobial administration should be intentionally withheld until all appropriate specimens have submitted to the microbiology laboratory. However, in critically ill patients, (e.g., sepsis, bacterial meningitis, febrile neutropenia, and ventilation associated pneumonia), empiric therapy should be initiated immediately after or concurrently with collection of diagnostic specimens.
- **Appropriate antimicrobial regimen selection and administration of initial antimicrobial therapy**
    - Since microbiologic reports on culture and sensitivity are reported after 24-72 hours, initial therapy for infection is often empiric and guided by the clinical presentation.

  - A common approach is to use broad-spectrum antimicrobials as initial empiric choices (occasionally combinations of agents) with intent to cover various possible pathogens commonly associated with the specific clinical syndrome.
  - Inadequate empiric therapy of infections in critically ill (e.g., sever sepsis & septic shock) is associated with poor outcomes.
  - For infections such as community-acquired pneumonia or cellulitis in the ambulatory setting where specific microbiological tests are not typically indicated, narrower spectrum antimicrobials should be directed on the most likely pathogens for the appropriate duration of therapy.
- The choice of initial empiric therapy depends on the following factors
  - The site of infection and the clinical syndrome
  - Immunological status of patient and underlying illness
  - Previously history of patient colonization or infection,
  - Prior hospitalization and antibiotic use history (previous 3 months),
  - Drug allergies
  - Setting in which the infection developed/acquired (i.e., home, or hospital)
  - Epidemiology, susceptibility patterns of bacteria in the hospital and ICU (antibiogram data),
  - Resistance potential of the likely pathogen,
  - Pharmacokinetics and dynamics of the chosen antimicrobial agent,
  - Toxicities and cost of chosen medication.
  - AWaRe categorization of the chosen medication
- **Antimicrobial combinations**

Although single-agent antimicrobial therapy is generally preferred, 2 or more combination agents are recommended in a few scenarios:

- For synergistic activity against a microorganism:
    - Example: combination of a Beta-lactam and an aminoglycoside exhibit synergistic activity against common pathogens causing infective endocarditis (Viridan streptococci): penicillin or ceftriaxone with gentamicin is used. Monotherapy is not generally recommended.
- **For critically ill patients before microbiological etiology and/or antimicrobial susceptibility determined**
    - Example: when a hospitalized patient develops septic shock and a gram-negative organism is suspected or grown, it would be apt to offer initial treatment with 2 antibiotics a combination of an antipseudomonal b-lactam with a fluoroquinolone or aminoglycoside. However, de-escalation of therapy is recommended based on microbiologic reports within 3 days.
- **For polymicrobial infections**
    - Example: most intra-abdominal infections are usually caused by multiple organisms with a variety of gram-positive cocci, gram-negative bacilli, and anaerobes. A Combination of a third-generation cephalosporin or a fluoroquinolone plus metronidazole is used.
- **To prevent emergence of resistance:**
    - This approach is well established for tuberculosis and the human immunodeficiency virus (HIV). However, this approach is not used for regular bacterial infection as it results in selection and spread of resistant strains.
- **Factors to be considered in selecting and administering antimicrobials**
    - Antimicrobial regimen selection is usually affected by the clinical and microbiologic diagnosis, severity of the illness, the host factors, prescriber knowledge, patient attitude, availability and cost of antimicrobials, pattern of antimicrobial resistance, antimicrobial policy and commercial influence.

- **Host factors to be considered in selection and administration of antimicrobials**
  - **Renal and hepatic function**
    - The kidneys and the liver are primary organs for drugs elimination.
    - Patients with reduced renal or hepatic function will accumulate certain antimicrobials unless dosage is adjusted.
    - Renal dose adjustment based on calculated eGFR is needed for a number of antimicrobials e.g. amphotericin b, tenofovir, vancomycin, aminoglycosides, some beta-lactams, fluoroquinolones
    - Some antimicrobials are nephrotoxic; hence may needed to be avoided in patients with underlying kidney disease e.g., amphotericin b, tenofovir, vancomycin, aminoglycosides,
  - **Age**
    - Drugs act differently in both extremes age patients, primarily due to differences in body physiology and organ function (e.g., kidney and liver).
    - Most pediatric drug dosing should be guided by weight as recommended by reference guidelines.
    - In geriatric patients, the serum creatinine level alone is not completely reflective of kidney function, and GFR should be calculated.
  - **Genetic Variations**
    - Abacavir has potentially fatal hypersensitivity reaction in individuals with the human leukocyte antigen allele HLA-B*5701.
    - Drugs like dapsone, primaquine, and nitrofurantoin can cause hemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficient patients. Hence, clinical follow up is needed if G6PD status is unknown.

- **History of allergy or intolerance**
    - A history of antimicrobial allergy or intolerance should be routinely considered in the evaluation and management of infection.
    - Currently it is believed that most penicillin allergy labels might not be actually correct.
    - In remote or unknown history of allergy or a mild cutaneous reaction: oral-challenge procedures may be safe.
    - Among penicillin allergic patients, cross reactivity with cephalosporins is ≤ 2% of the, except for allergy to aminopenicillins like amoxicillin and ampicillin (25-30%).
    - In penicillin allergic patients, a skin test and a challenge with carbapenems are acceptable.
    - For a patient, with sever (including sever delayed) or immediate (anaphylactic) reactions with beta lactam drugs, clindamycin, macrolides or floroquinolones can be used.
- **Pregnancy and Lactation:**
    - Check appropriate guidelines for safety before prescribing any antimicrobial.
    - Penicillins and cephalosporins: generally safe in pregnancy.
    - Macrolide: generally safe but a potential risk of miscarriage
    - Sulfonamides (e.g., trimethoprim-sulfamethoxazole) and nitrofurantoin: association with birth defects
    - Floroquinolones, tetracyclines and chloramphenicol: well-described fetal or neonatal adverse effects and should be avoided.
- **History of recent antimicrobial use and hospitalization**
    - Recent hospitalization for at least two days in the previous 90 days is a risk factors for acquiring resistant infections.

- **Drug related factors to be considered in selection and administration of antimicrobial agents**
  - **Bactericidal vs bacteriostatic**
    - Bactericidal antimicrobials are preferred to achieve rapid cure for serious infections such as meningitis and endocarditis.
  - **Pharmacodynamics characteristics:**
    - Specifically, this relates to the concept of time-dependent vs concentration-dependent killing.
    - Antimicrobials that exhibit time-dependent activity (b- lactams, vancomycin), and macrolides) have relatively slow bactericidal action.Their efficacy will be improved by administering either via continuous infusion or frequent dosing.
    - Antimicrobials that exhibit concentration-dependent killing (aminoglycosides, fluoroquinolones, metronidazole and rifampicin. The "peak" serum concentration is better associated with efficacy of these agents.
  - **Efficacy at the site of infection**
    - Antimicrobials will have an effect in a given site of infection, if they can achieve adequate concentration (≥ the MIC)
    - Antimicrobial concentrations achieved at some specialized sites like the CSF, bone, prostate, ocular fluid and abscess cavity are usually much lower than serum levels.
    - Example: Macrolides and first and second-generation cephalosporins (except cefuroxime) do not cross the blood-brain barrier and thus not used in CNS infections.
- **Drug effect monitoring:**
  - Most antimicrobials have wide therapeutic indexes that allow predictable dosage modifications.
  - Certain antimicrobials may require monitoring of serum levels. Examples: Aminoglycosides, vancomycin

  - Given the therapeutic drug monitoring capabilities are lacking in our setting, clinicians should be vigilant when using antimicrobials which require monitoring.

- **AWaRe category of antibiotics:**
  - AWaRe stands for ACCESS, WATCH and RESERVE, classification system introduced in 2019 by WHO.
  - The Ethiopian EML-2020 has adopted WHO's AWaRe classification with modifications.
  - **ACCESS** group antibiotics: e.g., penicillin, first generation cephalosporins, macrolides
    - They have activity against a wide range of commonly encountered community acquired pathogens.
    - They are widely used empiric treatment options as first- or second -choice for specific infectious syndromes like community acquired pneumonia.
  - **WATCH** group antibiotics: e.g., third and fourth generation cephalosporins, most fluoroquinolones, Ampicillin + Sulbactam
    - These are preferred first- or second -choice for specific serious infectious.
  - **RESERVE** group antibiotics e.g., Vancmycin, piperacillin + tazobactam, meropenem, meropenem/vaborbactam, ceftazidime/avibactam, colistin, Polymyxin B)
    - These should be reserved for treatment of confirmed or suspected infections due to multi drug-resistant organisms.
    - They are recommended to be used for "High Priority" pathogens notably MRSA (vancomycin) and carbapenem resistant enterobacteriaceae.

- **Follow-up assessment (Stop and assess)**
  - De-escalation

  - Once microbiology results identify the etiologic pathogen and/or antimicrobial susceptibility data are available, all attempt must be made to narrow the antibiotic spectrum.

- ○ **Intravenous to oral change**
  - The oral route is the widely preferred route for outpatient settings.
  - For hospitalized patients the IV is preferred until the patient improves and becomes stable enough to take orally.
  - Hospitalized patients with mild to moderate infections in which the main reason for the hospitalization is not the infection (e.g., heart failure) are still candidates for oral antimicrobial agents as far as they are able to take orally.
  - Oral therapies for invasive systemic infections should have excellent absorption and bioavailability e.g., amoxicillin-clavulanate, first-generation cephalosporins, fluoroquinolones, clindamycin, metronidazole.
  - Oral therapy is less reliable and not recommended for serious infections, such as infective endocarditis and central nervous system infections (e.g., meningitis), that require high serum or CSF drug concentrations.

- ○ **Duration of antimicrobial therapy**
  - The duration of therapy for many infections has long been controversial.
  - Given the harmful effects of prolonged antimicrobial use, after minimum duration assessing for a possible discontinuation is needed.
  - Currently shorter treatment duration is advocated
  - Carefully individualizing the treatment durations based on response is needed.

FURTHER READING

A. Surbhi Leekha, Christine L. Terrell, and Randall S. Edson. Mayo Clin Proc. 2011;86(2):156-167.

B. Shira Doron, and Lisa E. Davidson. Antimicrobial Stewardship. Mayo Clin Proc. 2011;86(11):1113-1123

8.3 ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

8.3.1 DIAGNOSIS AND MANAGEMENT OF ARV NAVE PATIENTS

BRIEF DESCRIPTION

- AIDS is a chronic infectious disease caused by the *Human Immunodeficiency Virus* (HIV) types 1 and 2.
- It is essentially a disease of the immune system.
- It leaves the individual susceptible for various types of infections and the development of malignancies.
- The most advanced stage of HIV infection is called AIDS.
- AIDS is defined by the development of certain cancers, infections, or other severe clinical manifestations.

TRANSMISSION

- Sexual contact (major means),
- Direct contact to contaminated blood and blood products and
- From infected mother to child.

CLINICAL FEATURES

- Variable depending on the degree of immunodeficiency (clinical stage of disease).

- The first few weeks after initial infection, individuals may experience no symptoms or an influenza-like illness including fever, headache, rash or sore throat.
- At advanced immunodeficiency, patients are at a very high risk of being infected with less virulent organisms (opportunistic infections).
- Refer below for a list of clinical conditions in the four WHO stages of HIV and at the end of this topic for the management of each opportunistic infection (OIs).

INVESTIGATIONS AND DIAGNOSIS

- Demonstration of antibodies to HIV by Rapid test using the National HIV test algorism using rapid diagnostic tests (RDTs) (figure 1)
- HIV antigen detection
- Direct detection of the virus using PCR

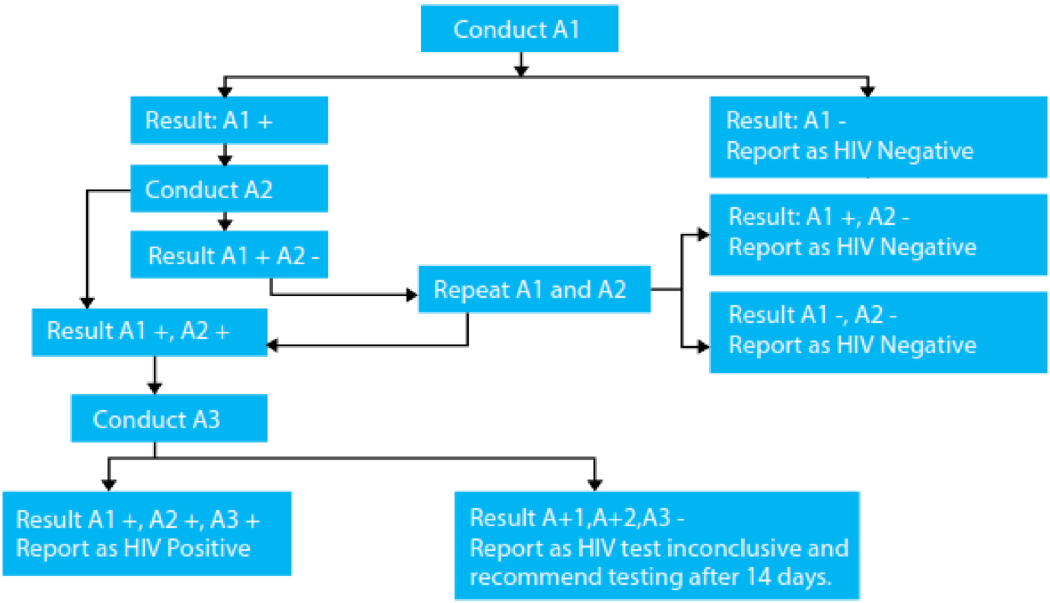
Conduct A1
Result: A1 +
Result: A1 -
Report as HIV Negative
Conduct A2
Result A1 + A2 -
Result: A1 +, A2 -
Report as HIV Negative
Repeat A1 and A2
Result A1 -, A2 -
Report as HIV Negative
Result A1 +, A2 +
Conduct A3
Result A1 +, A2 +, A3 +
Report as HIV Positive
Result A+1,A+2,A3 -
Report as HIV test inconclusive and recommend testing after 14 days.

Figure 8.1: Recommended HIV testing strategy for Ethiopia (source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

CLINICAL STAGES OF HIV DISEASE AS PER WORLD HEALTH ORGANIZATION (WHO) CLASSIFICATION

- **Clinical Stage 1**
  - Asymptomatic infection
  - Persistent generalized lymphadenopathy
  - Acute Retroviral (HIV) Syndrome
  - Performance Status 1: asymptomatic, normal activity
- **Clinical Stage 2**
  - Unintentional weight loss < 10% body weight
  - Minor mucocutaneous manifestations (e.g., PPE seborrheic dermatitis, prurigo, fungal nail infections, angular cheilitis)
  - Herpes zoster within previous 5 years
  - Recurrent upper respiratory tract infections
  - Performance Status 2: symptoms, but nearly fully ambulatory
- **Clinical Stage 3**
  - Unintentional weight loss > 10% body weight
  - Chronic diarrhea > 1 month
  - Prolonged fever > 1 month (constant or intermittent)
  - Oral candidiasis
  - Oral hairy leukoplakia
  - Pulmonary tuberculosis within the previous 2 years
  - Severe bacterial infections
  - Vulvovaginal candidiasis
  - Unexplained anemia, neutropenia or chronic thrombocytopenia

  - Performance Status 3: in bed more than normal but < 50% of normal daytime during the previous month

- **Clinical Stage 4**
  - HIV wasting syndrome
  - Pneumocystis carinii pneumonia
  - Toxoplasmosis of the brain
  - Cryptosporidiosis with diarrhea > 1 month
  - Isosporiasis with diarrhea > 1 month
  - Cryptococcosis, extrapulmonary
  - Cytomegalovirus disease of an organ other than liver, spleen or lymph node
  - Herpes simplex virus infection, mucocutaneous
  - Progressive multifocal leukoencephalopathy
  - Any disseminated endemic mycosis (e.g., histoplasmosis)
  - Candidiasis of the esophagus, trachea, bronchi, or lung
  - Atypical mycobacteriosis, disseminated
  - Non-typhoid Salmonella septicemia
  - Extrapulmonary tuberculosis
  - Lymphoma
  - Kaposi's sarcoma
  - HIV encephalopathy
  - Visceral Leishmaniasis
  - HIV –associated cardiomyopathy
  - HIV-associated nephropathy

- Performance Status 4: in bed > 50% of normal daytime during previous month
- Treatment

OBJECTIVE

- Suppress viral replication to undetectable levels durably;
- Restore and preserve immunologic function;
- Prevent HIV transmission;
- Prevent opportunistic infections;
- Rehabilitate the patient and allow full function and survival.

NON PHARMACOLOGIC

- Counseling and psychological support
- Nutritional support
- Socio-economic support

PHARMACOLOGIC

- Management of HIV disease includes prevention and treatment of OIs and controlling viral replication with Highly Active Antiretroviral Therapy (HAART).

Note: All confirmed HIV positive patients should be enrolled on the pre-ART register initially until they start ART and transferred to ART register as soon as they start the ART.

GENERAL CONSIDERATIONS FOR ANTI-RETROVIRAL THERAPY (ART)

When to start treatment

- Initiate ART as early as possible (same day to within seven days of HIV diagnosis) and this significantly reducing HIV related morbidity and mortality, and reducing forward transmission of HIV including mother to child transmission (MTCT).

- All HIV positive people are eligible for ART irrespective of their WHO clinical staging and/or CD4 count following a confirmed HIV diagnosis, clinical assessment and assessment of client readiness.
- As a priority, ART should be initiated as early as possible in all adolescents and adults with advanced disease (WHO stage 3 to 4, CD4 count ≤350 cells/mm3) and all children regardless of WHO staging and CD4 count/ percentage
- For women identified at labor and delivery, provide ART with in the same hour of HIV diagnosis with brief counseling and provide detailed counseling on ARV and adherence after delivery.

MEDICINE REGIMENS

First-line regimens for adults and adolescents in Ethiopia: for treatment naive patient for the first time or those with advanced HIV disease.

- **TDF/3TC/DTG or TDF/3TC/EFV as a once-daily dose**

NB; Current evidence-based guidelines do not recommend NNRTI (e.g., EFV) based regimen as firs line options due to the availability of more tolerable and efficacies INSTI (DTG, BIC, RAL) containing regimens.

- Fixed-dose combinations and once-daily regimens are preferred.
- Previous guideline does not recommend DTG containing regimens for pregnant and breast feeding and women of childbearing age due to preliminary NTD report of 0.9% from Botswana. Advanced reports show 0.3% NTD risk still higher than the non-DTC regimens NTD risk (0.1%). Based on this evidence DTG can be used as the alternative preferred agent for women of childbearing potential after discussing the potential risk with the mother.
- For HIV/TB co-infected adults and adolescents, the recommended dose of DTG is 50 mg twice daily.

MANAGEMENT OF ADVANCED HIV DISEASE

- For adults and adolescents, and children older than five years, advanced HIV disease is defined as CD4 cell count <200cells/mm3 or WHO stage 3 or 4 event.

- All children younger than five years old with HIV are considered as having advanced HIV disease.
- A package of interventions including screening, treatment and/or prophylaxis for major OIs, rapid ART initiation and intensified adherence support should be offered to everyone presenting with advanced HIV disease including those who are reengaging with care after a period of interruption.
- **Recommended first line ARV Regimens unless there are contraindications:**
    - ***Preferred:*** regimen is the same as above, TDF+3TC+ DTG or EFV

RE-ENGAGING WITH CARE AFTER ART INTERRUPTION

- Re-evaluate for possible adherence barriers and advanced clinical conditions.
- Then resume the same (previous) ART regimen used before interruption. However, people interrupting NNRTI – containing regimen (high risk of drug resistance) should restart using a DTG- containing regimen (has high genetic barrier to resistance and can bring rapid viral suppression).
- Then, ongoing Enhanced Adherence Counseling (EAC), frequent follow-up, close viral load monitoring/determining at 3 and 6 months after resuming ART is required. If the two consecutive viral load is >1000copies/ml, switch to second- or third-line regimen.

8.3.2 DIAGNOSIS AND MANAGEMENT OF ARV FAILURE

- Seek an expert advice if there is a treatment failure
- Clinical, immunologic and virologic evaluations are required to determine treatment failure
- Routine viral load testing is a more sensitive and earlier indicator of treatment failure.

- o To detect treatment failure proactively, routine viral load (VL) testing should be done at 6 and 12 months of initiating ART and then every 12 months thereafter and plus whenever there is clinical or immunologic suspicion of treatment failure.
- o If a VL of > 1000copies/ml on routine or need-based VL test, address adherence issues by identifying adherence barriers and by providing enhanced adherence support (EAS) for 3-months;
- o Virologic failure evaluation should include adherence assessment, drug-drug and drug-food interactions, drug tolerability, HIV RNA level and CD4 cell count trends over time, ART history, and prior and current drug-resistance test results (if test available).
- o VL above 1000 copies/ml based on 2 consecutive VL measurements in 3 months, with EAS following the first VL test is indicative of treatment failure and hence a regimen changes to second- or third-line agents.

Table 8.8: Definitions of clinical, immunological and virological failure for the decision to switch ART regimens in adults and adolescents (source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

Failure	Definition	Remark
Clinical failure	• New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition and certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure) after 6 months of effective treatment.	• The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART.

Immunologic failure	• CD4 count at or below 250 cells/mm3 following clinical failure or • Persistent CD4 levels below100 cells/mm3.	• Without concomitant or recent infection to cause a transient decline in the CD4 cell count. Persistent is to mean at least 2CD4 measurements below the threshold. • Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure.
Virologic failure	• Viral load above 1000 copies/ml based on two consecutive viral load measurements in 3 months, with enhanced adherence support following the first viral load test.	• An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed. VL testing should not be done when there is an acute infection/fever.

ENHANCED ADHERENCE SUPPORT (EAS)

- EAS is important if have unsuppressed VL, persisted or new immunosuppression, developing new OI or have multiple adherence barriers. It shall be systematic and with documenting the interventions provided during the EAS period

Table 8.9: Summary of components of enhanced adherence counselling (EAC or EAS) (source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Enhanced adherence counselling sessions overview	
Session1	• Review cognitive, behavioural, emotional and socio-economic barriers to adherence: • Treatment literacy • Medications: dosage, timing, storage • Side effects • Discuss risk reduction (e.g., for substance abuse) • Motivation • Mental health screening (for depression and other common mental problems using national mental health assessment tool (Annex 13) • Discuss patient's support systems • Referrals and networking. • Assist patient to develop adherence plan to address the identified issues.
Session2	• Review adherence plan from the first session and discuss any challenges. • Identify other possible gaps and issues emerging. • Referrals and networking. • Assist patient to modify the adherence plan to address the identified issues.

Session3	• Review adherence plan from the first and second session and discuss any challenges. • Identify other possible gaps and issues emerging. • Assist patient to modify the adherence plan to address the identified issues. • Decision on repeat VL based on current adherence: • If the adherence is good: plan repeat VL testing after three months of good adherence and explain possible ways forward, emphasizing role of the patient and the health facility. • If adherence challenges persist: plan further EAC sessions before repeating the VL.
Session to discuss on repeat viral load results	• Discuss result of the second VL test with the patient. • Plan the way forward: • 1. If VL now < 1,000: continue current regimen with enhanced adherence • 2. For those patients with identified significant adherence barriers, it is advisable to extend the provision of EAC for 6 months before doing the second VL testing in order to properly address the barriers and give optimal time for viral suppression to happen

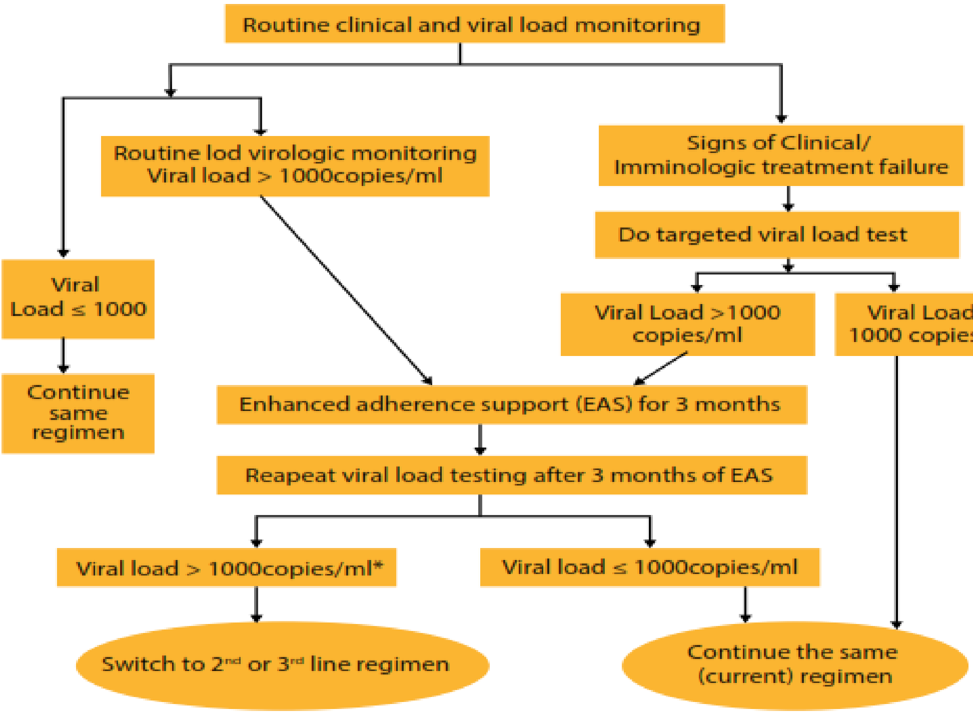
Routine clinical and viral load monitoring
Routine lod virologic monitoring Viral load > 1000copies/ml
Signs of Clinical/ Imminologic treatment failure
Do targeted viral load test
Viral Load ≤ 1000
Continue same regimen
Viral Load >1000 copies/ml
Viral Load ≤ 1000 copies/ml
Enhanced adherence support (EAS) for 3 months
Reapeat viral load testing after 3 months of EAS
Viral load > 1000copies/ml*
Viral load ≤ 1000copies/ml
Switch to 2nd or 3rd line regimen
Continue the same (current) regimen

Figure 8.2. Algorithm for routine clinical and viral load monitoring.

** For those patients with identified significant adherence barriers, it is advisable to extend the provision of EAC for 6 months before doing the second VL testing in order to properly address the barriers and give optimal time for viral suppression to happen.* (Source: *National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018*)

Second-line ARV combination regimens for adults and adolescents

- Before switching to second (as well as third) line regimen, ensure the following.
  - Two consecutive viral load measurements > 1000 copies/ml at least 3 months apart.
  - First viral load measurement done at least 6 months after switching to second-line regimen.
  - The repeat VL test should be done after 3 months of EAS.

- A new regimen for treatment experienced patients should include at least two, and preferably three, fully active agents (Fully active agents: have uncompromised activity based on patient's ART history and drug-resistance test results, if available or have a novel mechanism of action).
- Provide continuous adherence support to all patients before and after regimen changes.
- Discontinuation or a briefly interruption of therapy will lead to a rapid increase in HIV RNA, a decrease in CD4 count, and an increase in the risk of clinical progression.
- Using an INTIs or boosted PI + two NRTI combinations is recommended as the preferred second-line ART for adults, adolescents and also for children when NNRTI- containing regimens were used in first-line ART.
- If a boosted PI plus two NRTIs failure, an INSTI based or another boosted PI plus two NRTIs will be a preferred agent.
- If an INSTI plus two NRTIs failure, switch to Boosted PI plus two NRTIs

Table 8.10:preferred second-line ART regimens for adults and adolescents (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Target population	**Preferred second-line regimen for first line treatment failure**	
Adults and adolescents (≥10 years)[a]	If TDF+3TC+DTG-[b]used in first-line	AZT + 3TC + ATV/r or LPV/r
	If AZT was used in first-line ART	TDF + 3TC + DTG[b] or LPV/r or ATV/r
	If TDF was used in first-line ART	AZT + 3TC + DTG[b] or LPV/r or ATV/r
HIV and TB co- infection	If rifabutin is not available	Same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily) or standard LPV dose with an adjusted dose of RTV (that is, LPV/r 400 mg/400 mg twice daily).

HIV and HBV co-infection	DTG + TDF/3TC + ATV/r OR AZT + TDF + 3TC + (ATV/r or LPV/r)	If switching an ARV regimen in HBV/HIV coinfected patients, HBV active ARV drugs (TDF/3TC) should be continued in the new regimen. Discontinuation of HBV active ARV drugs may lead to reactivation of HBV and result in serious hepatocellular damage. The DTG regimen may be preferred if the loose AZT is unavailable. If DTG regimen used, watch increased hepatotoxicity of DTG and HBV
Any	Failed second line regimen	Refer

a Adult clients taking ABC can be shifted to AZT. For pregnant *women same regimens recommended as for adults and adolescents, but cautious counseling or alternative suggestions (if available) is required before DTG use (low NTD risk of 0.3% vs 0.1 % in non DTG regimens). If TDF and ABC have been used in the first-line regimen, patients may be referred to experienced physicians for selection of the second-line medicines.*

b For HIV/ TB co-infected adults and adolescents, the recommended dose of DTG is 50 mg twice daily. Children weighing more than 20 kg can take adult 50mg film-coated tablets, RAL can be used in neonates and children less than 20 kg body weight.

Identification and management of second-line treatment failure

- Patients who are on second-line regimen and have high viral load level (>1000copies/ml) after 6 months of treatment need to go through the algorithm as described for first line treatment failure with EAS and repeat test after three months to decide second line treatment failure.
- If confirmed to have second line failure, consider referring to hospital with experienced physicians for initiation of third line regimens.

(Refer Table 3.14 of the National consolidated Guideline for comprehensive HIV prevention, care and treatment (2018), for Summary of sequencing options for preferred first, second and third-line ART regimens in adults, adolescents, pregnant women and children)

DOSING FOR ARV REGIMENS IN ADOLESCENTS AND ADULTS

See **Table 8.11** for the dosing recommendations

- Once or twice daily dosing is preferred in order to enhance adherence to therapy.
- Use the heat stable tablet of LPV/r (200/50mg).
- Atazanavir/ritonavir has equivalent efficacy to LPV/r and has advantage of being given once a day and in patients with dyslipidemia.
- Medicine hypersensitivity and high-level cross-resistance to long term use of thymidine analogues (ZDV) are concerns when using ABC.
- TDF can be compromised by multiple nucleoside analogue mutations (NAMs) but often retains activity against some nucleoside-resistant viral strains. It is also administered once daily.

Table 8.11: Dosage of anti-retroviral medicines for adults and adolescents (recommendations are for normal renal and hepatic functions as well as irrespective of drug interaction)

Medicine class/Medicine	Dose
Nucleoside & Nucleotide RTI's	
Tenofovir (TDF)	300 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (ZDV)	250–300 mg twice daily
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Non-Nucleoside RTI's	
Efavirenz (EFV)	400-600mg once daily

Nevirapine (NVP)	200 mg once daily for 14 days, then 200mg twice daily
Etravirine (ETV)	200 mg twice daily
Protease inhibitors	
Atazanavir/ritonavir (ATV/r)	300mg/100mg once daily
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily (for individuals with no previous PI) or 600 mg + 100 mg twice daily (for individuals with previous PI use)
Lopinavir/ritonavir (LPV/r)	400mg/100mg twice daily (533mg/133mg twice daily when combined with EfV or NVP)
	Considerations for individuals receiving TB therapy
	In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjusted dose of LPV/r: LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily). OR, SQV/r (SQV 400 mg + RTV 400 mg twice daily), with close monitoring.
Integrase strand transfer inhibitors (INSTIs)	
Dolutegravir (DTG)	50 mg once daily, If TB coinfection, 50mg BID
Raltegravir (RAL)	400 mg twice daily

8.3.3. MONITORING ARV TREATMENT

- Start from the day of initiation.
- The first six months of therapy are especially critical for monitoring.

WHAT TO EXPECT IN THE FIRST MONTHS OF ART AND HOW TO MANAGE THEM?

- ART initiation may be associated with immune reconstitution inflammatory syndrome (IRIS) as well as early adverse drug events, such as drug hypersensitivity, in the first three months of ART

- Be alert to OIs and/or IRIS as well as adverse drug events, in the early phase of ART initiation.
- Especially a high mortality seen in the first three to six months of ART initiation among people who started ART with advanced HIV disease with existing co-infections and/or co- morbidities, severely low hemoglobin, low body mass index (severe malnutrition) and/or very low CD4 counts.
- Failure to achieve CD4 recovery or presence of CD4 decline after treatment initiation particularly after one year (common in those with very low CD4 cell on ART initiation) should alert to potential adherence problems or primary non-response to ART, and consideration should be given to continue prophylaxis for OI such as CPT till patients recovers immunologically.

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

- IRIS is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to ART.
- It occurs among 10–30% of the people initiating ART, usually within the first 4–8 weeks after initiating therapy.
- It may present in two different ways: paradoxical IRIS (an OI or tumor diagnosed before ART, initially responds to treatment but then deteriorates after ART starts); or unmasking IRIS (initiating ART triggers disease that is not clinically apparent before ART).
- It should be considered only when the presentation cannot be explained by a new infection, expected course of a known infection or drug toxicity.
- The most serious and life-threatening forms of paradoxical IRIS are for TB, Cryptococcus's, Kaposi's sarcoma and hepatitis.
- BCG vaccine–associated IRIS (localized and systemic) may occur in some HIV infected infants.
- Before initiating ARV, give due consideration for patients with low CD4 cell count (<50 cells/mm3) at ART initiation, disseminated OIs or tumors

and a shorter duration of therapy for OIs before ART starts as they are the main risk factors for IRIS.

- IRIS is not indicative of treatment failure or drug side effect.
- It is generally self-limiting, and interruption of ART is rarely indicated, but people may need to be reassured in the face of protracted symptoms to prevent discontinuation of or poor adherence to ART.

(NB: Actively watch for IRIS in patients starting with first-line regimens containing INTIs such as DTG)

- The most important steps to reduce the development of IRIS include
    - Earlier HIV diagnosis and initiation of ART before a decline to below 200 CD4 cells/mm^3;
    - Improved screening for OIs before ART, especially TB and Cryptococcus; and
    - Optimal management of OIs before initiating ART.
- Timing of ART in people with OIs requires balancing a greater risk of IRIS after early initiation against continuing high mortality if ART is delayed.
- Investigation and diagnosis of IRIS
- Most or all of the following features should be present in order to make the diagnosis of IRIS
    - A low pretreatment CD4 count (often < 100 cells/μL) except in tuberculosis. IRIS secondary to preexisting TB infection may occur in individuals with CD4 counts >200;
    - A positive immunological response to ART;
    - The absence of evidence of drug-resistant infection, bacterial super infection, drug allergy or other adverse drug reactions, patient noncompliance, or reduced drug levels due to drug-drug interactions or mal-absorption after appropriate evaluation for the clinical presentation;

  - The presence of clinical manifestations consistent with an inflammatory condition; and
  - A temporal association between HAART initiation and the onset of clinical features of illness- usually within the first 6 months.

MANAGEMENT OF IRIS

- Patients should generally be treated for the underlying OI as soon as possible.
- Continuation of ART when IRIS occurs.

ANTI-INFLAMMATORY AGENTS' VS IRIS

- Particularly helpful in settings of obstructive mass lesions (e.g., expanding cervical lymph node).
- Their use, particularly corticosteroids, must be weighed against potential risks/side effects.
- If corticosteroids, initiate therapy with prednisone at a dose of 1 mg/kg/day (maximal dose 60 to 80 mg) followed by a rapid taper over a 10 to 14-day period.
- IRIS in closed spaces (e.g., CNS OI) should be managed promptly or referred to appropriate center to avert significant morbidity and mortality.
- Clinical and laboratory monitoring including baseline assessments
- Standardized clinical assessment of patients and, when available baseline CD4 count,are important to determine the severity of immunosuppression and decide on initiation of prophylactic therapies.
- Before initiating ART, patients shall be thoroughly evaluated at baseline and periodically for the rest of their lives to monitor toxicity, intolerance, poor response or failure to treatment.
  - OIs including TB, Cryptococci infection and other co-morbidities are always need to be looked for and managed.
  - This clinical assessment should include possible medicine interactions (e.g. with contraceptives, ant-tuberculosis medicines), patient-caregiver

partnership, commitment to long-term treatment and adherence to medicine therapy, any perceived side-effects, and maintenance of safe sexual practices.

- Once on ART: follow-up visits and evaluation recommendations
    - Every one week for the first two consecutive visits and a gradual extension.
    - Then, every two weeks during the first month of treatment
    - Every 4 weeks (every month) then after until 24 weeks of treatment.
    - After the 24th weeks of initiation of ART, schedule patients to return every 12 weeks.
- NB: Patients should be encouraged to come at any time if they have concerns and can be seen out of the above schedule whenever necessary.
- During each visit, patient should be evaluated for new symptoms that may be related to
    - Medicine side effects,
    - Che disease progression, and
    - Clinical improvements/deterioration, and
    - Adherence,
    - Development of OIs or recurrent problems that may exist.
- When a woman in reproductive age is taking an ARV combination regimen:
    - Consider the available safety, efficacy, and PK data on use during pregnancy for each agent.
    - The risk and benefits of ARV use should be discussed in line with the most current Perinatal Guidelines when designing a regimen.
    - Based on recent data, DTG containing regimen have a low risk of NTD (0.3%) but still, higher than a non-DTG containing regimens (0.1%).
    - DTG NTD risks may be higher in areas with poor folic acid fortification program

- Use DTG should be made after carefully considering the risk of infant NTDs risks of taking DTG if pregnancy occurs, and the risks of persistent viremia in the patient and potential HIV transmission to the fetus if pregnancy occurs while the patient is not on effective ART.

MONITORING FOR TOXICITY OF ART

Guiding principles

- Establish whether the clinical condition is due to ARV toxicities, other drugs, or other illness including new OIs.
- Try to identify the responsible ARV drug.
- Assess the severity using toxicity grading matrix (Table 8.12, 8.13)

CLINICAL MONITORING FOR TOXICITY OF ART (TABLE 8.12)

- The major causes of drug discontinuation in the first 3-6 months after initiating ART are due to drug toxicities; and hence, they must be closely monitored.
- They occur from few weeks to months.
- All patients require clinical evaluation at least every month in the first 6 months for ARV related toxicity.

LABORATORY MONITORING FOR TOXICITY OF ART (TABLE 8.13):

- **Baseline:**Hemoglobin/hematocrit, WBC count and differential, serum alanine aminotransferase, serum creatinine and/or blood urea nitrogen, serum glucose, pregnancy test. If resources permitting: serum bilirubin, amylase, triglycerides, and cholesterol.
- **Follow-up:** The above investigations need to be repeated bi-monthly, particularly at the start of treatment. Once stabilized, investigations may then be performed every three months and at any time when they are indicated.

Table 8.12: Grading of toxicity in adults and adolescents (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

Item	Grade I (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grade 4 (Severe life-threatening)
Peripheral neuropathy	• Transient or mild discomfort, no limitation of activity. • No medical intervention/ treatment required.	• Moderate limitation of activity, some assistance might be needed. • Non-narcotic analgesia required.	• Marked limitation in activity, some assistance usually required, medical intervention/therapy required, and hospitalization possible. • Severe discomfort and/ or severe impairment (decrease or loss of sensation up to knees or wrists) narcotic analgesia required.	• Extreme limitation in activity, significant assistance required, significant medical intervention/ therapy required, hospitalization/ hospice care. • Incapacitating or not responsive to narcotic analgesia. • Sensory loss involves limbs and trunk.

Cutaneous/Rash/ Dermatitis	• Erythema, pruritus	• Diffuse, maculopapular rash or dry desquamation	• Vesiculation or moist desquamation or ulceration	• Erythema multiforme or suspected Stevens-Johnson syndrome or Toxic Epidermal • Necrolysis (TEN).
Management	• Continue ARV; provide careful clinical monitoring; and consider change of a single drug • if condition worsens.		• Substitute responsible drug	• Stop ARV and consult experienced physician.

Table 8.13: Laboratory grading of adverse events in adults and adolescents (ACTG) (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

Variable	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hemoglobin	8.0-9.4 g/dL	7.0-7.9 g/dL	6.5-6.9 g/dL	<6.5 g/Dl
Absolute Neutrophil Count	1,000-1,500 mm3	750-990 mm3	500-749 mm3	<500 mm3

Platelets	-75,0000-99,000	50,000-74,999	20,0000-49,999 mm3	<20,000
ALT	1.25-2.5 X upper normal limit	2.5-5 X upper normal limit	5.0-10 X upper normal limit	10 X upper normal limit
Bilirubin	1-1.5 X ULN	1.5-2.5 X ULN	2.5-5 x upper limits of normal	>5 x upper limits of normal
Amylase/ lipase	1-1.5 X ULN	1.5-2 X ULN	2-5 x upper limits of normal	>5x upper limits of normal
Tri-glycerides *	200-399mg/dL	400-750 mg/dL	751-1200mg/dL	>1200mg/dL
Management	Continue ARV; Repeat test 2 weeks after initial test and reassess		substitute responsible drug	Stop ARV and consult experienced physician
Cholesterol * 1.0 –1.3 X Upper normal limit; 1.3-1.6 X Upper normal limit; 1.6-2.0 X Upper normal limit; 2.0 X Upper normal limit Lipid imbalances could be managed with diet, exercise and pharmacologically with the use of fibrates.				
	ALWAYS SEEK EXPERT ADVICE IN CASE OF DOUBT			

Grade 1 (Mild reaction): are bothersome but do not require changes in therapy

Grade 2 (Moderate reaction): consider continuation of ART as long as feasible. If the patient does not improve in symptomatic therapy, consider single-drug substitution.

Grade 3 (Severe reaction): Substitute offending drug without stopping ART. Closely monitor using laboratory and clinical parameters.

Grade 4 (Severe life-threatening reaction): Immediately discontinue all ARV drugs, manage the medical event with symptomatic and supportive therapy, and reintroduce ARV drugs using a modified regimen (i.e., with an ARV substitution for the offending drug) when the patient is stabilized. Life-threatening toxicity includes severe hepatitis, pancreatitis, lactic acidosis or Steven-Johnson syndrome.

(Refer Table 3.7 of the National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018 for types of toxicities associated with first, second and third-line ARV drugs)

DRUG INTERACTIONS (TABLE 8.14, 8.15)

- Providers should be aware of all drugs that people with HIV are taking when ART is initiated and new drugs that are added during treatment maintenance.
- Acid-reducers (PPIs, H2 antagonists, or antacids) can decrease the absorption of ARV drugs requiring gastric acidity for optimal absorption (i.e., atazanavir and rilpivirine).
- Polyvalent cation containing products (supplements, iron products, or antacids containing aluminum, calcium, or magnesium) can bind and reduce absorption of INSTIs (e.g., DTG).
- Cytochrome P450 (CYP) 3A4 or efflux transporter P-glycoprotein inducers or inhibitors may reduce or promote the absorption and/or effect of other drugs.

(Please refer other pertinent sources for interaction of ARV medications with Hepatitis C, Hepatitis B and Cytomegalovirus antiviral agents)

Table 8.14: Key ARV drug interactions and suggested management (modified from the National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

ARV drug	Key interactions	Effect; and Suggested management
TDF	nephrotoxics [e.g., ampho- B, aminoglycoside, ganciclovir, pentamidine, vancomycin or interleukin 2]	*Exacerbate nephrotoxicity;* Avoid concurrent use
	ritonavir boosted PIs	Closely monitor renal function
AZT	Ribavirin and pegylated interferonalpha-2a	Substitute with TDF
	Atovaquone	*ZDV AUC ↑ 31%;* Monitor for ZDV-related adverse effects.
DTG	Carbamazepine, Phenobarbital and phenytoin	Use alternative anticonvulsant agent
	EFV	*DTG AUC ↓ 57% and Cmin ↓ 75%* DTG 50 mg twice daily
	Polyvalent Cation products containing Mg, Al, Fe, Ca, and Zn	*Absorption of DTG or RAL is affected/ reduced* Use DTG or RAL at least 2 hrs before or at least 6 hrs after supplements containing polyvalent cations, including but not limited to – Fe-, Ca-, Mg-, or Zn-multivitamin; mineral supplements, cation containing laxatives and Al-, Ca- or Mg- containing antacids. Monitor for virological efficacy.
RAL	Polyvalent Cation products containing Mg, Al, Fe, Ca, and Zn	

NVP	Rifampicin	Substitute NVP with EFV
	Itraconazole and ketoconazole	*Low antifungal concentration to sub therapeutic level* Use an alternative antifungal agent (for example fluconazole)
	Methadone	Adjust methadone dose as appropriate
	Astemizole and terfenadine	Use alternative antihistamine agent
	ATV Unboosted; ATV/c	Do not coadminister
EFV	Amodiaquine	Use an alternative antimalarial agent
	Methadone	Adjust methadone dose as appropriate
	Estrogen-based hormonal contraception	Use alternative or additional contraceptive methods
	Astemizole and terfenadine	Use an alternative anti- histamine agent
	ATV	Not coadminister with ATV Unboosted **ATV/c in ART-Naive Patients:** - ATV 400 mg + COBI 150 mg once daily - Not use coformulated ATV 300 mg/ COBI 150 mg. **ATV/c in ART-Experienced Patients:** - Do not coadminister. Not coadminister **ATV/r** in ART-experienced patients No dose adjustment needed for EFV.

Boosted PI (ATV/r, LPV/r)	Rifampicin	Substitute rifampicin with rifabutin, Adjust PI dose or substitute with 3 NRTIs (for children)
	Lovastatin and simvastatin	*Increase concentration* Use alternative dyslipidemic agent (e.g., pravastatin)
	Halofantrine and lumefantrine	Use an alternative antimalarial agent
	Estrogen-based hormonal contraception	Use alternative or additional contraceptive methods
	Methadone and Buprenorphine	Adjust methadone and buprenorphine doses as appropriate
	Astemizole and terfenadine	Use alternative antihistamine agent
Other PI	TDF	Do not coadminister unboosted ATV with TDF. Use ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicities if used with **DRV/c or ATV**.
NB: Be aware that PIs do have an extensive drug interactions that require avoiding co-administration or dose modification or frequent clinical monitoring with the following class of medications: Anticonvulsants, cardiac drugs (particularly anti-arrythmics), gastric acid reducing agents (PPIs may need to be avoided in most cases), Alpha-Adrenergic Antagonists, Macrolides (except Azithromycin), anticoagulants, antiplatelets, antidepressants/anxiolytics, antipsychotics, antifungals, antimalarials, anti-asthmatics, and other multiple drugs. Please refer pertinent resources.		

Table 8.15: Drug-drug interactions (ARVs and anti-TB drugs for treatment of DR-TB) (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Clinical Condition	Responsible ARV drug/s	Responsible anti TB drug/s	Recommendations
Bone marrow suppression	AZT	Lzd, R, H	Monitor blood counts regularly. Replace AZT if bone marrow suppression occurs. Consider suspension of Lzd. Also consider cotrimoxazole, if patient is taking.
Hepatotoxicity	NVP, EFV, protease inhibitors, NRTIs	H, R, E, Z, Bdq, PAS, Eto/ Pto, FQ	When severe, stop both the ART and TB medications, and restart the TB medications first. Consider cotrimoxazole, if patient is taking. Also rule out viral hepatitis (Hepatitis A, B, C & Cytomegalovirus (CMV)).
Renal toxicity	TDF	Aminoglycosides, Cm	TDF may cause renal injury. If possible, avoid TDF in patients receiving aminoglycosides or Cm. If TDF is absolutely indicated, serum creatinine and electrolytes should be monitored (at least every two weeks). Even without the concurrent use of TDF, PLHIV have increased risk of renal toxicity secondary to aminoglycosides and Cm. In the presence of renal insufficiency, ARV and anti- TB medications need to have their doses adjusted.

Central nervous system (CNS) toxicity	EFV	Cs, H, Eto/ Pto, FQ	EFV has a high rate of CNS side effects in the first 2–3 weeks of use, but typically self-limited and resolves. At present, there are limited data on the use of EFV with Cs; concurrent use is the accepted practice with frequent monitoring for central nervous system toxicity. Psychosis can occur with Cs, but is rare with EFV alone; other causes should always be ruled out.
QTc Prolongation	Protease inhibitors (PIs) LPV/r	Bdq, Dlm, Mfx, Gfx, Cfz, Lfx, Ofx	PIs may result QTc prolongation. The additive effects of combining ART with known second- line anti-TB drugs, on QTc prolongation is not known. Close monitoring is indicated.
Dysglycaemia (disturbed blood sugar regulation)	Protease inhibitors (PIs)	Gfx, Eto/ Pto	Protease inhibitors tend to cause insulin resistance and hyperglycemia. Eto/ Pto tends to make insulin control in diabetics more difficult, and can result in hypoglycemia and poor glucose regulation.
For patients who are co-infected with HIV and MDR/XDR-TB, there is limited information on interactions of ARV drugs with new drugs such as bedaquiline and delamanid. Concomitant use of all PIs with bedaquiline may interfere with drug concentrations (↑ bdq serum level) and not recommended unless benefits outweigh; alternative ARV options should be considered, if possible. Monitor liver function and ECG for QTc prolongation. **Rifampin or Rifapentine** should never be co-administered with all PIs. Consider rifabutin150 mg once daily if a rifamycin is indicated.			

MONITORING EFFECTIVENESS OF ART

- Response to ART is monitored using both clinical and laboratory parameters (See treatment section above for the definitions of treatment failure).
- Clinical Parameters: (new or recurrent conditions, body weight, OIs and HIV related malignancies)

- The concentration of HIV RNA in plasma (the "viral load")
- CD4+ cell count

8.3.4 POST-EXPOSURE PROPHYLAXIS (PEP) AND CARE

- Universal precaution is the most effective way of protecting individuals from accidental transmission of HIV and other blood borne pathogens especially among high-risk groups such as health care givers.

STEPS TO MANAGE POTENTIAL HIV EXPOSED PERSON

- **Treat the exposure site /immediate measures/**
  - Percutaneous injury or injury to non-intact skin:
    - Wash exposed site with soap & water as soon as possible, without scrubbing.
    - Avoid using antiseptics.
    - Allow free bleeding but do not squeeze the wound.
  - Exposed mucous membranes or eye:
    - Irrigate copiously with clean water or saline.
- **Report the exposure:**
  - To PEP focal person or ART physician or nurse in the facility immediately to handle the case based on the national programmatic recommendations
- **Start PEP:**
  - PEP is a medical emergency - If possible, administer the first dose within 2 hours of exposure.

PEP recommendations based on risk assessment (Table 8.16 and 8.17)

- PEP is indicated for occupational exposures with a percutaneous, mucous membrane and non-intact skin exposure with potentially infectious body fluids.
- If the HIV status is unknown, starting empiric PEP and confirming the source patient HIV status is very critical to weight the benefit against the cost of treatment continuation.
- If the source patient is inaccessible for HIV testing for any reason, empiric PEP is recommended regardless of the knowledge of HIV status particularly for high-risk exposure settings or high-risk source patients. For instance, if the source is at high risk for HIV infection (eg, injection drug users) or has symptoms suggesting HIV infection or risky exposure setting (e.g., needle stick from a sharps container in an HIV clinic).

Table 8.16: Recommended PEP based on risk assessment.

Source HIV status	Recommendations to potential infectious body fluid occupational exposure*
Source patient is HIV positive (symptomatic or asymptomatic)	3 drug PEP (preferred regimen: *TDF +3TC+DTG*) **
Source patient HIV status is unknown	Give 3 drug PEP while awaiting HIV testing
Source patient is HIV negative	No PEP warranted

*Infectious body fluids include *blood, semen, vaginal secretions, any body fluids contaminated with visible blood, as well as cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids are potentially infectious. On the other hand, feces, nasal secretions, saliva, gastric secretions, sputum, sweat, tears, urine, and/or vomitus are not considered infectious unless they contain blood;* **3 drug PEP preferred over two drug regimen and should be given within 72 hours for 28 days.

Table 8.17: Recommended ARVs for PEP and administration guide (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

ARV drug regimen	Dose	Frequency	Duration
3-Drug Regimen: Triple FDC (TDF/3TC/DTG)	Triple FDC (TDF 300mg, 3TC 300mg, DTG 50mg)	Once daily	28 days Raltegravir (400 mg BID) or boosted PI based regimen may be used in pregnant mothers
Tenofovir (TDF)/ Zidovudine (AZT) + Lamivudine (3TC) + **Lopinavir/ritonavir (LPV/r)** **or** **Atazanavir/ritonavir (ATV/r)**	AZT 300mg 3TC 150mg	12 hourly	28 days
	LPV/r400mg/100mg	12 hourly	28 days
	ATV/r300mg/100mg	Once daily	28 days

TIMING AND DURATION OF INITIATION OF PROPHYLAXIS:

- PEP is a medical emergency.
- To be effective, PEP should commence as soon as possible (within 1-2 hours).
- However, do not consider PEP beyond 72 hours post exposure.
- Prophylaxis is to be given for 28 days.

TESTING AND MONITORING AFTER OCCUPATIONAL EXPOSURE:

Testing source:

- Rapid HIV test for the source is necessary. If the source is negative no need for further assessment of the exposed victim is needed. If the source is positive, tasting the exposed person is needed.
- For test negative sources with any suggestive HIV symptoms, virologic testing is recommended.
- HIV serology test of the exposed person: immediately after exposure.
- If the result is positive no need for PEP, but if negative administer PEP as soon as possible as outlined above and then repeat serology at 6 weeks, 3 months, and 6 months.
- Testing of exposed person (health care worker) for possible HBV in line with national viral Hepatitis guideline is also recommended.

NB: initiate PEP immediately after exposure until test result confirms the HIV status of the victim. Stop PEP if the health worker is positive for HIV antibodies.

Following HIV exposure there is a need for psychosocial support.

PREVENTION OF TRANSMISSION OF HIV AFTER SEXUAL ASSAULT

- Need counseling about potential risk of HIV infection
- Know the victim's HIV status prior to PEP
- Encourage patient to be tested as early as possible with a delay not > 72 hours
- Inform possibility of transmitting infection during sero-conversion
- Instruct to return at 6 weeks and 3 months post sexual assault for voluntary counseling and HIV testing.
- Post-rape prophylaxis should be monitored & evaluated for:

  - Emergency contraceptives
  - Psychosocial and legal support
  - Screening for conventional STIs and follow-up management
  - Drug side effects
  - Sero-conversion
- Recommended PEP for post sexual Assault HIV exposure
  - AZT or TDF + 3TC + DTG for 28 days.
  - Alternatively, Kaletra or boosted Atazanavir can substitute DTG **(see Table 8.17 above)**

FOLLOW-UP OF CLIENT EXPOSED TO HIV

- **Post exposure testing**
  - A client who is taking PEP should be followed in adult ART clinic
  - Instruct to return at 6 weeks, 3 months and 6 months post sexual assault for voluntary counseling and HIV testing.
- **Monitoring and management of PEP toxicity**
  - Reassessed within 3-5 days for medication tolerability and toxicity.
  - A further risk assessment re-evaluation may also be appropriate as necessary
  - Drug toxicity should be tested at baseline and again 2 weeks after starting PEP.
  - The scope of testing is based on medical conditions of candidate and toxicity of drugs included in PEP regimen.
  - Minimal, lab monitoring for toxicity includes CBC and LFT.
  - If toxicity is noted, modification of regimen should be considered.

8.3.4 PRE-EXPOSURE PROPHYLAXIS (PREP)

- Oral PrEP of HIV is the use of ARV drugs by people who are not infected with HIV but at a substantial risk.
- Substantial risk of HIV infection is defined as incidence of HIV higher than 3 per 100 person-years in the absence of PrEP.
  - HIV-positive sexual partner, recent bacterial STI, high number of sex partners, history of inconsistent or no condom use and commercial sex work; In high HIV prevalence area or network; HIV-positive injecting partner sharing injection equipment.
- PrEP is aimed to block the acquisition of HIV.
- **Eligibility for PrEP**
  - Negative HIV test result before prescribing PrEP
  - No signs/symptoms of acute HIV infection
  - Normal renal function; no contraindicated medications
  - Known hepatitis B virus infection and vaccination status
- **Prescriptions for PrEP and follow-up**
  - Daily, continuing, oral doses of TDF+3TC or FTC, ≤90-day supply
  - Follow-up visits at least every 3 months to provide the following:
    - HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment
    - At 3 months and every 6 months thereafter, assess renal function
    - Every 3-6 months, test for bacterial STIs

8.3.5 MANAGEMENT OF COMMON CO-INFECTIONS OF HIV

- Screening and management of opportunistic infections (OIs) is critical at any time of HIV care.
- Frequently affected organ systems are the nervous, gastro-intestinal and respiratory systems, and the skin.
- In general, milder infections such as herpes zoster and other skin infections occur early whereas serious life-threatening infections such as CNS toxoplasmosis and Cryptococcal meningitis occur later with severe immune-suppression. Some life-threatening infections, such as pneumonia and TB, may occur early as well as later. When TB occurs later it is atypical, more disseminated and more extra pulmonary

GENERAL STRATEGIES TO PREVENT OPPORTUNISTIC INFECTIONS ARE:

- Reduction of exposure
- Chemoprophylaxis (primary/secondary)
- Immunization and
- Starting HAART

CO-TRIMOXAZOLE PREVENTIVE THERAPY (CPT)

- CPT should be initiated for prevention of Pneumocystis pneumonia, toxoplasmosis, bacterial infections and diarrhea caused by Isospora belli or Cyclospora species, as well as benefits for malaria prophylaxis (**See Tables 8.18 to 8.19 below)**

Table 8.18: CPT indication for primary prophylaxis (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

Age	Criteria for initiation	Criteria for discontinuation*	Monitoring approach
≥5 years, including adults	Any WHO stage and CD4 count ≤350 cells/mm3 OR WHO stage 3 or 4, irrespective of CD4 level	Discontinue in clinically stable patients (individuals on ART for at least one year without any new WHO clinical stage 2, 3 or 4 events) with; •Evidence of immune recovery and/or viral suppression (CD4 count >350 cells/mm3, with viral load suppression) or • Two consecutive CD4 count > 350 cells/mm3 if no VL result	Clinical at 3-month intervals

**Discontinue also if the person has Stevens-Johnson syndrome, severe liver disease, severe anemia, severe pancytopenia or negative HIV status. Contraindications to CPT: severe allergy to sulfa drugs; severe liver disease, severe renal disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency.*

Table 8.19: Dosage of co-trimoxazole for adults and adolescents (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Age (weight)	Suspicion (240 mg/5ml co- trimoxazole)	Single strength tab (480 mg of Co-trimoxazole)	Double strength tab (960 mg of co- trimoxazole)
>14 yrs (>30 kg)		2tab/day	1 tab/day

Table 8.20: Adverse effects of CPT and management (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Toxicity	Clinical description	Recommendation
Grade 1	Erythema, pruritis	Prescribe anti-histamine and continue CPT and close follow-up.
Grade 2	Diffuse maculopapular rash, dry desquamation	Prescribe Anti-histamine and continue CPT and close follow-up.
Grade 3	Vesiculation, minor mucosal ulceration	STOP CPT, manage and re-introduce after 2 weeks with observation (desensitize).
Grade 4	Exfoliative dermatitis, Steven-Johnson syndrome or erythema multiforme, moist desquamation	STOP CPT; NEVER Restart Co-Trimoxazol

RESPIRATORY SYSTEM OPPORTUNISTIC DISEASES

Tuberculosis

- TB is the most frequent life-threatening OI and a leading cause of death in HIV infected people.
- TB increases HIV replication through immune activation, thus high viral load and rapid progression of HIV disease.
- On the other hand, HIV increases susceptibility to M. tuberculosis infection (20-37 times greater lifetime risk than HIV negative), progression to TB disease and the incidence and prevalence of TB.
- This necessitates collaboration among the two programs.

NATIONALLY RECOMMENDED TB/HIV COLLABORATIVE ACTIVITIES

- Strengthen mechanisms for integrated TB and HIV services delivery and surveillance
- Reduce burden of TB in HIV infected people and initiate early ART (the three I's i.e., Intensive TB case finding, isoniazid preventive therapy (IPT) and TB infection control)
- Reduce the burden of HIV in patients with presumptive and diagnosed TB by testing, counseling, preventive therapy, treatment and continuous care;

Table 8.21: Timing of ART for adults and children with TB (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

Patients with tuberculosis found to be HIV positive	HIV positive patients taking ART diagnosed with TB
• Start ART in all TB patients, including with drug-resistant TB, irrespective of the CD4 count. • Start anti-TB treatment first, followed by ART as soon as possible within the first 8 weeks. If profound immune-suppression (such as CD4 count < 50 cells/ mm3),ART should be started immediately within the first two weeks of initiating TB treatment.	• Start anti-TB • Modify ART regimen to avoid drug-drug interaction • Evaluate for treatment failure

INTENSIFY TB CASE FINDING AND ENSURE QUALITY TB TREATMENT

- All HIV positive clients should be informed about risk of developing active TB and the advantages of being screened for TB.
- Adults and adolescents living with HIV who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases.

- Children living with HIV who have any of the symptoms of poor weight gain, fever, current cough or contact history with TB case may have active TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, children should be offered IPT, if no contraindications, regardless of their age.

(Refer for the screening methods in children and adults from the National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

DIAGNOSIS OF TB IN HIV INFECTED PEOPLE

- Standard TB diagnostic approaches and clinical algorithms should be followed to guide the diagnosis of TB in PLHIV.
- **XPert MTB/RIF Test (GeneXpert Test)**
    - Is recommended as an initial diagnostic test for all presumptive TB cases (individuals with TB symptoms) among HIV infected people.
- **AFB microscopy (**2 spot tests with in 1 hour**):** if access to XPert MTB/RIF test is limited.
- **Chest radiography**
- **Sputum culture:** In patients with XPert negative results, sputum culture may be indicated.

DIAGNOSIS OF EXTRA-PULMONARY TUBERCULOSIS IN HIV POSITIVE

- Extra-pulmonary tuberculosis is more HIV-related than pulmonary TB.
- The accurate diagnosis of extra-pulmonary tuberculosis is complex and difficult, particularly in peripheral health facilities with limited diagnostic capacity.
- Therefore, it is important for healthcare workers to have high-index of suspicion and critically evaluate through clinical algorithms.

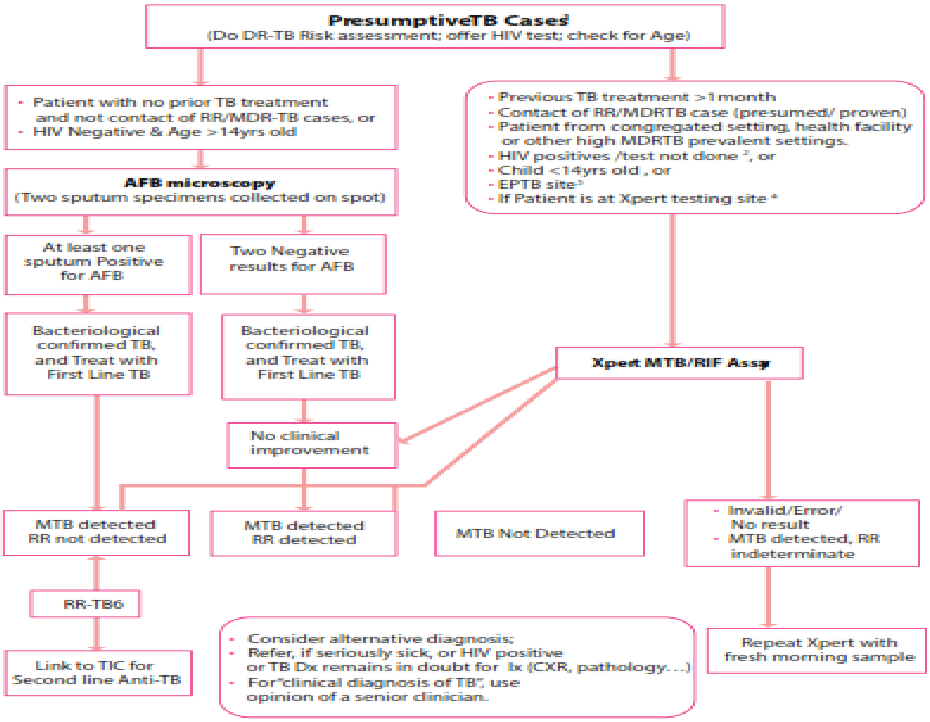
PresumptiveTB Cases¹
(Do DR-TB Risk assessment; offer HIV test; check for Age)
- Patient with no prior TB treatment and not contact of RR/MDR-TB cases, or
- HIV Negative & Age >14yrs old
AFB microscopy
(Two sputum specimens collected on spot)
At least one sputum Positive for AFB
Two Negative results for AFB
Bacteriological confirmed TB, and Treat with First Line TB
Bacteriological confirmed TB, and Treat with First Line TB
No clinical improvement
- Previous TB treatment >1month
- Contact of RR/MDRTB case (presumed/ proven)
- Patient from congregated setting, health facility or other high MDRTB prevalent settings.
- HIV positives /test not done ², or
- Child <14yrs old , or
- EPTB site³
- If Patient is at Xpert testing site ⁴
Xpert MTB/RIF Assay
MTB detected RR not detected
MTB detected RR detected
MTB Not Detected
- Invalid/Error/ No result
- MTB detected, RR indeterminate
RR-TB6
Link to TIC for Second line Anti-TB
- Consider alternative diagnosis;
- Refer, if seriously sick, or HIV positive or TB Dx remains in doubt for Ix (CXR, pathology….)
- For"clinical diagnosis of TB", use opinion of a senior clinician.
Repeat Xpert with fresh morning sample

Figure 8.3: Algorithm for the diagnosis of extrapulmonary tuberculosis (source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

- Presumptive TB is defined as having symptom and signs consistent with TB; mainly persistent cough of two or more weeks (or cough of any duration if HIV positive).
- For patients in whom "HIV test is not done" at time of TB evaluation, Xpert test may be the initial test if the clinician has strong clinical suspicion of HIV infection or if the patient possesses risk behavior to acquire HIV infection.
- Liquid specimens from EPTB site (in particular CSF) may be subjected to Xpert test without additional processing.
- Xpert test is preferred test to examine presumptive TB patients identified at facility where the machine is available.

- Broad spectrum antimicrobials, excluding fluoroquinolone or anti-TB drugs is to be given for 10-14days.
- RR-TB result in patients considered to be low risk for MDR-TB warrants DR-TB risk re-assessment and a repeat Xpert test on fresh specimen, and if result shows RR-TB again; link the patient to TIC for Second line TB treatment; but if the repeat test result identifies TB but not RR-TB, initiate first line TB regimen as bacteriologically confirmed susceptible TB at TB clinic.

Note:

- Xpert MTB/RIF test is recommended as initial diagnostic test for CSF in patients presumed to have TB meningitis.
- One sputum sample for the facility which have Xpert test and two samples for sample referring facilities
- Antibiotic trial: has a role to treat concomitant bacterial infection for PLHIV with cough or serious illness, but not helpful in the diagnosis of TB in HIV positives.

Table 8.22: Extra pulmonary TB diagnostic approaches in HIV positive patients (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Type of TB	Evidences Strongly Suggestive of EPTB	Investigations and recommendations
Lymph node TB	2cm or more in size, Asymmetrical/ localized; Painless swelling; Firm/ fluctuated; Cervical location; patient with weight loss, night sweats, fever	LN Aspirate for AFB has 85% yield, if not possible to do FNAC of LN, start anti-TB.

Pleural effusion	Unilateral effusion; Aspirate of fluid is clear and straw colored and clots on standing in a tube without anti- coagulants or pleural fluid analysis shows protein >30g/L &>50% lymphocytes; Patients with weight loss, night sweats, fever, or evidence of TB elsewhere	Start anti-TB as soon as possible.
Tuberculosis Meningitis	Patients with weight loss, night sweats, fever; Cerebrospinal fluid clear with high protein, low glucose and lymphocytes; Cryptococcal antigen (or Indian Ink and fungal culture) negative in CSF Evidence of TB elsewhere	Admit patient, start anti-TB with steroids as soon as possible. Start treatment for cryptococcal meningitis based on clinical or lab evidences. Note: GeneXpert test has to be conducted on CSF specimen as an initial diagnostic test as much as possible.
Pericardial Effusion	Hemodynamically significant pericardial effusion, often with pleural effusions, Lung fields clear and intra-thoracic lymphadenopathy. Usually patients with weight loss, night sweats, fever. N.B. 90% of Pericardial Effusions in HIV positive patients in high-TB burden areas is due to TB.	CXR, Echocardiograph or chest ultrasound; pericardiocentesis, and pericardial biopsy; routine TB Workup. Start anti-TB as soon as possible
Disseminated TB	Patients with weight loss, night sweats, fever and cough; Abnormal CXR (which can include miliary pattern); Large spleen/liver, Anemia	Start anti-TB treatment (add antibiotics if critically ill)

TB of the Spine	Pain over localized area, children/ adolescents –often thoracic vertebrae. Adults: frequently lumbar vertebrae.	Spinal imaging (e.g., X-Ray, MRI); FNA of vertebral lesions and/or paraspinous abscesses when feasible.

TB PREVENTION WITH ISONIAZID PREVENTIVE THERAPY

- Screening for exclusion of active TB in HIV infected persons is the single most important step that should precede the decision to initiate IPT.
- Providing IPT to people living with HIV does not increase the risk of developing INH-resistant TB and should not be a barrier to providing IPT.
- The dose of INH is 300mg/day for adults and 10mg/kg for children. The duration of IPT is for six months.
- Vitamin B6 (25mg/day) can be provided to prevent INH-induced peripheral neuropathy.

CONTRAINDICATIONS OF IPT

- Individuals with any one or more of the following conditions should not receive IPT:
    - Symptoms compatible with tuberculosis even if the diagnosis isn't yet confirmed.
    - Active hepatitis (chronic or acute)
    - Regular and heavy alcohol consumptions
    - Prior allergy or intolerance to isoniazid
    - Symptoms of peripheral neuropathy

NB: Past history of TB and current pregnancy should not be contraindications for starting IPT.

NATIONAL POLICY:

- IPT should be administered at enrolment to HIV care after ruling out active TB.
- IPT is to be administered once and should not be repeated unless there is strong indication on its benefits which is to be decided by senior physician.
- IPT should be administered only for six months.
- IPT should not be administered right after completing full course of TB treatment
- IPT can be administered for patients who had history of TB treatment before three years.

FOLLOW-UP OF PATIENTS ON IPT

- Given monthly supply of Isoniazid for the first three months and three months' supply for the remaining months.
- They will be assessed at each follow-up visit to:
  - Evaluate adherence to treatment and to educate client.
  - Evaluate for drug toxicity.
  - Evaluate for signs and symptoms of active tuberculosis or other OI.
  - Stop IPT if active TB is diagnosed and to immediately start anti-TB.

IPT TREATMENT INTERRUPTION MANAGEMENT

- An interrupting client should be traced (by adherence case managers/ adherence supporters, HEW or through the index person) and treatment must be resumed after identifying and addressing the adherence barriers.
- IPT is said to be completed if a patient completed the full course of therapy within nine months period (i.e., the six months doses should be finished in nine months' time).
- If the client discontinues treatment for a period of less than three months:
  - Resume the same course by adding for the missed doses at the end.

- If the client discontinues treatment for a period of more than three months:
    - o Re-initiate new course of IPT for six months.

REPETITION AND PROLONGATION OF IPT:

- Repeating IPT after the first cycle of IPT or the provision of IPT after completion of full course of TB therapy is not recommended in Ethiopia.

Provide HIV testing and counseling to presumptive and confirmed TB patients

- Among TB-HIV co-infected patients, other OIs are significant causes of morbidity and mortality even with a successful treatment of TB, necessitating routine HIV testing and counseling to all TB patients.

PRESUMPTIVE TREATMENT OF TB FOR PEOPLE LIVING WITH HIV

- To prevent the death of people with HIV in situations where expedited diagnosis of TB is not possible or feasible due to the clinical condition of the patient or limited access to TB diagnostic services.
- No case definition for presumptive TB.
- WHO algorithms include initiation of TB treatment for people with HIV in peripheral facilities based exclusively on clinical suspicion (without TB investigations) for seriously sick patients (with respiratory distress) based on the judgment of the clinician.
- However, every effort should be made to confirm the diagnosis of TB after initiation of presumptive treatment and that treatment should be stopped only if there is bacteriological, histological or strong clinical evidence of an alternative diagnosis.

INTRODUCE HIV PREVENTION INTERVENTIONS FOR PRESUMPTIVE AND CONFIRMED TB PATIENTS

- All clients attending TB clinics should be screened for STI using a set of simple questions.

- Those with symptoms of STI should be treated or referred to the treatment providers. (Refer to the National Guideline for the Treatment of STI using the Syndromic Approach)
- Condoms should be made available in TB clinics.

PROVIDE CO-TRIMOXAZOLE PREVENTIVE THERAPY FOR HIV POSITIVE TB PATIENTS

- CPT is recommended to all TB/HIV co-infected patients regardless of their CD4 Count.
- All PLHIV with TB and receiving CPT should be registered on the unit TB register, as well as the Pre ART/ART Register. They should also be monitored monthly.

Ensure HIV prevention, treatment and care for HIV positive TB patients

- Health units should be equipped with protective materials and routinely follow standard precautions to prevent HIV transmission in the healthcare settings.
- Linkage should be ensured for pregnant and non-pregnant HIV positive clients to access services for prevention of mother to child transmission.
- TB clinics should link to HIV services to provide the continuum of care and support for HIV positives during and after completion of anti-TB treatment.

MANAGEMENT CONSIDERATION FOR TB/HIV CO-INFECTIONS

- Treatment of suspected TB for individuals with HIV is the same as for individuals without HIV. However, the DTG should be used on BID bases.
- Ant-TB must be provided first, followed by ART as soon as possible within the first 8 weeks of treatment.
- While the patient is immediately enrolled to HIV chronic care, should receive TB care at the TB clinic for the duration of TB treatment.
- Appropriate clinical, psychosocial and laboratory evaluations as per the national guidelines for ART should be performed as soon as possible.

MULTIDRUG-RESISTANT TB AND HIV

- Xpert MTB/RIF is the preferred test where possible,
- The burden of MDR-TB can be reduced by strengthening HIV prevention, improving infection control and collaboration between HIV and TB control activities, with special attention to the groups at the highest risk of MDR-TB and HIV infection, such as people who inject drugs and those exposed in congregate settings.
- Refer for the management of MDR-TB section

BACTERIAL PNEUMONIA

- Bacterial pneumonia tends to be more severe and recurrent as the CD4 counts drops significantly.
- Pneumonia can also concomitantly present with sinusitis and/or bacteremia.
- If not treated promptly, extra pulmonary complications like empyema, meningitis, pericarditis, hepatitis and arthritis can follow.
- Streptococcus pneumonia and Haemophiles influenzae are the most common etiologies of community onset.

CLINICAL MANIFESTATION

- Sudden onsets of cough, sputum production, chest pain, fever and/or shortness of breath are typical presentations.

SEVER PNEUMONIA:

- Tachypnea (RR>30/minute), old age (>70 years), cyanosis, hypotension, systolic blood pressure <80mm Hg, multi-lobar involvement and altered mental status in adults, and chest in-drawing, grunting and presence of danger signs in children.
- Tachypnea for children: Birth to 2 months RR >60/minute, 2 months to 1 year RR> 50/minute, 1 year to 5 years > 40 and 5 years and above RR> 30/minute.

DIAGNOSIS

- Acute symptoms presented over days to a few weeks and/or abnormal physical signs of systemic infection and consolidation in the affected lung/s should raise suspicion.
- Radiologic imaging assists in confirming the diagnosis of pneumonia.

TREATMENT

- **Refer the management for pneumonia section elsewhere in this guideline.**

PNEUMOCYSTIS PNEUMONIA

- Caused by Pneumocystis jiroveci, formerly known as pneumocystis carini pneumonia, a ubiquitous classified as a fungus but also have characteristics of protozoa.
- It frequently causes pneumonia among immuno-compromised individuals.
- It commonly occurs when patients have significant immune suppression (CD4<200cells/mm3 or CD4 percentage < 14%).

CLINICAL MANIFESTATION

- Typical have an insidious (sub-acute onset over 2 to 4 weeks) onset of low-grade fever, dry cough, fatigue and progressive dyspnea exacerbated by exertion.
- Patients will have an increasing tachypnea, tachycardia and cyanosis as the disease progresses.
- Physical examination reveals fever, tachypnea, tachycardia and scattered rales in the lungs but examination of the lungs can appear normal in some patients.
- In children highest incidence is seen between 2-6 months of age and is characterized by abrupt onset of fever, tachypnea, dyspnea and cyanosis.

INVESTIGATIONS AND DIAGNOSIS

- Due to non-specific presentation, PCP should always be considered in those patients with evidence of moderate to severe immunosuppression who come up with cough, progressive dyspnea or fatigue.

- **Chest X-ray**: presumptive diagnosis of PCP is based on clinical judgment and typical chest X-ray findings revealing a perihilar interstitial infiltration with tendency to spread outwards. Note that the chest X-ray can be normal in 20% of patients.
- **Culture**: definitive diagnosis of PCP. Induced sputum sample using special stains like Giemsa or methylamine silver stains, but these tests are not routinely done in Ethiopia.

TREATMENT OBJECTIVES

- Suppress multiplication of the organism
- Relieve symptoms.

Non pharmacologic

- Oxygen should be given in moderate and severe cases.

Pharmacologic

- Patients who develop PCP despite **TMP-SMX** prophylaxis usually can be treated effectively with standard doses of **TMP-SMX**

First line: Trimethoprim **+ Sulphamethoxazole for 3 weeks**

- **Trimethoprim+Sulphamethoxazole, 15-20mg/kg/day based on the trimethoprim component and administered in three or four divided doses for 21 days. Usual dosage 2 double strength (960mg), P.O., TID.** Give the same medicine IV if the patient is not able to swallow the medicine and shift orally when tolerable.
- Close monitoring is necessary during the initial five days of treatment and if patient grows sicker, administration of oxygen is useful.
- In severely ill patients with marked respiratory distress and extensive chest X-ray findings, prednisolone has to be given simultaneously until completion of intensive co-trimoxazole therapy.

- Toxicity of co-trimoxazole, like skin rash, bone marrow suppression, hepatitis and renal failure can be troublesome in some patients with advanced HIV disease and requires close monitoring. Steven Johnson syndrome may occur if the patient is allowed to take the medicine after the development of rash.
- Secondary prophylaxis after completion of the course of treatment with co-trimoxazole should be continued (see secondary prophylaxis section below).

Alternative

- Clindamycin+ Primaquine or Dapsone for 3 weeks
- Clindamycin, 300-450mg P.O., TID (600 mg BID) for 3 weeks PLUS Primaquine, 30mg base P.O., QD (15 mg BID) for 3 weeks. OR
- Clindamycin 600 mg qid plus dapsone 100 mg daily for 3 weeks. OR
- Pentamidine Isethionate, 4mg/kg I.V. QD for three weeks. It should be given to those who fail to tolerate the above regimen. OR
- Dapsone, 100mg P.O., QD for 3 weeks PLUS Trimethoprim, 20mg/kg administered P.O., in divided doses QID for 3 weeks.

N.B. Typically a mild rash with fever develops 7 to 10 days after initiation of therapy. Bone marrow suppression may occur, and CBC monitoring is useful. Possible hepato-toxicity and nephro-toxicity may also be evaluated at the third week of therapy.

- Consider spontaneous pneumothorax in patients with sudden deterioration in clinical condition.

ADJUVANT CORTICOSTEROIDS TREATMENT

- Indicated if SPO2< 90%, while breathing room air as measured by pulse oximetry before or in the course of treatment.
- In the absence of pulse oximetry, clinical judgment should be used to select moderately to severely sick patients who benefit from corticosteroids.
- Regimen
    - Prednisolone 40mg BID for 5 days,

  - Then 20mg BID for 5 days,
  - Then 20mg QD until therapy is complete (for 11 days).
  - No tapering from the 20 mg dose is necessary.
  - For severe PCP in children: prednisolone 2mg/kg per day for the first 7 - 10 days followed by a tapering regimen for the next 10 - 14 days.

SECONDARY PROPHYLAXIS:

- Indication: Prior PCP
- Preferred Therapy: Trimethoprim + Sulphamethoxazole, 1 DS tablet PO daily
- When to discontinue:
  - CD4 count increased from <200 cells/mm3 to >200 cells/mm3 for >3 months as a result of ART or,
  - if CD4 count is 100–200 cells/mm3 and HIV RNA remains below limits of detection of assay used for ≥3 months to 6 months
  - If PCP occurs at a CD4 count >200 cells/mm3 while not on ART, prudent to continue for life or discontinuation can be considered once HIV RNA levels are suppressed to below limits of detection of the assay used for ≥3 months to 6 months (limited data for this practice).
- When to restart secondary prophylaxis (same as for recommendations to restart primary prophylaxis, see below)

PREVENTING FIRST EPISODE OF PCP (PRIMARY PROPHYLAXIS):

- Indications:
  - CD4 count <200 cells/mm3 or
  - CD4 percentage <14% of total lymphocyte count or
  - CD4 count >200 cells/mm3, but <250 cells/mm3 if ART initiation must be delayed and if CD4 count monitoring (e.g., every 3 months) is not possible.

NB: Patients who are receiving TMP-SMX or pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP.

- Preferred Therapy:
  - TMP-SMX, 1 DS tablet PO daily or
- Alternative Therapy:
  - Dapsone 100 mg PO daily or dapsone 50 mg PO twice a day or Atovaquone 1500 mg PO daily with food
- When to discontinuing:
  - CD4 count increased from <200 cells/mm3 to ≥200 cells/mm3 for ≥3 months in response to ART, or
  - If CD4 count is 100–200 cells/mm3 and HIV RNA remains below limit of detection of the assay used for ≥3 months to 6 months
- When to restarting Primary Prophylaxis:
  - CD4 count <100 cells/mm3 regardless of HIV RNA
  - CD4 count 100–200 cells/mm3 and HIV RNA above detection limit of the assay used

PREGNANCY CONSIDERATIONS

- The management and the prophylaxis for pregnant is similar to non-pregnant mothers. TMP-SMX is the preferred drug in pregnant. However, be aware of the theoretical risk of teratogenicity in the first trimester with the use of TMP-SMX. Aerosolized pentamidine or oral atovaquone can be used as alternative than discontinuing chemoprophylaxis in the first trimester (see the "pregnancy consideration" section of Toxoplasma Gondi encephalitis for additional notes).

LYMPHOID INTERSTITIAL PNEUMONITIS (LIP)

- One of the most common chronic lower respiratory conditions occurring in up to 25% of children with HIV/AIDS

CLINICAL MANIFESTATIONS

- Ranges from asymptomatic disease with isolated radiographic findings to bullous lung disease with pulmonary insufficiency.
- Symptomatic children present with insidious onset of tachypnea, cough, and mild to moderate hypoxemia with normal auscultatory findings or minimal rales or wheezing.
- Progressive disease is accompanied by digital clubbing and symptomatic hypoxemia.
- Associated physical findings include generalized lymphadenopathy, hepatosplenomegaly and parotid enlargement.

DIAGNOSIS

- Usually based on clinical examination findings, diffuse bilateral reticulonodular infiltrate on X-ray with mediastinal lymphadenopathy.
- It is important to exclude tuberculosis and other infectious etiology.
- Treatment
- Symptomatic treatment (hydration, oxygen).
- Antibiotics: if there is a superimposed bacterial infection.
- Bronchodilators: may be helpful in mild to moderate disease.
- Corticosteroids: reserved for children with significant hypoxemia and symptoms of pulmonary insufficiency. Give prednisolone 1 – 2 mg/kg/24 hrs for 6 – 8 weeks and then taper as tolerated.

GASTROINTESTINAL (GI) OPPORTUNISTIC DISEASES

- GI OIs commonly manifest with diarrhea, nausea and vomiting, dysphagia and odynophagia among others.
- Most common causes among HIV infected are Isospora belli, cryptosporidium, shigella and salmonella, CMV etc.
- A scenario of multiple concurrent GI infections is fairly common.

- A number of drugs with similar effects can pose challenges in differential diagnosis.
- The general principle of managing Gastrointestinal OIs:
    - Identifying and treating the specific offending agent and
    - Providing supportive care to monitor situations such as fluid loss.

DYSPHAGIA AND ODYNOPHAGIA

- Dysphagia (difficulty in swallowing) and odynophagia (painful swallowing) are symptoms of esophagitis occurring at advanced stages of AIDS.
- They are usually caused by candida, HSV, CMV, and aphthous ulcers.
- As well as a sign of severe immunodeficiency, esophagitis also seriously impairs the patient's nutritional status.
- Therefore, prompt diagnosis and treatment are mandatory to avert nutritional complications and inability to swallow prescribed medications.
- Children will present with reluctance to eat, excessive salivation, or crying while feeding.
- If thrush is associated with dysphagia, odynophagia, and/or retrosternal pain, consider oesophageal candidiasis but this can also occur in the absence of oral thrush.

CANDIDA INFECTIONS

- Oral Candida infections (thrush): may occur in > 90% of HIV/AIDS patients in any time.
- Thrush or oropharyngeal candida is characterized by white, painless, plaque-like lesions on the buccal surface and/or tongue. It also has pain; decreased food and fluid intake.
- Candida esophagitis: majorly an extension of oral trash but not always an extension. It is characterized painful swallowing, obstructed swallowing, substernal pain

DIAGNOSIS

- It is frequently made on clinical grounds (signs and symptoms of infection),
- When facilities are available upper GI endoscopy with or without biopsy or contrast imaging and fungal cultures, potassium hydroxide smear may be done.

TREATMENT

- Dysphagia and/or odynophagia are treated as oesophageal candida on clinical grounds, in particular when oropharyngeal candida is present.
- Patients are empirically treated with Fluconazole in presumptive oesophageal candida.
- If the response is unsatisfactory, they should be referred or investigated if facilities are available, to rule out other causes.

Table 8.23: Gastrointestinal opportunistic infections management (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018)

	First line	Alternative	Duration
Oropharyngeal candidiasis	Fluconazole 100-200 mg orally daily (3mg/k/day in children) or Itraconazole 200 mg PO daily or ketoconazole 200 mg (3-6mg/kg/daydaily in children) BID	Posaconazole 400 mg PO daily (after twice daily on day 1) or miconazolebuccaltablets 50 mg PO daily or clotrimazole troches 10 mg PO five times daily or nystatin 5 mL (100,000 units/mL)-swish and swallow four or five times daily	7–14 days

Esophageal candidiasis	Fluconazole 100–400 mg PO or IV daily or itraconazole 200 mg PO daily	Voriconazole 200 mg PO or IV twice daily or Posaconazole 400 mg PO daily (after twice daily on day 1) or other azoles, or caspofungins, or amphotericin B	14–21 days
Vulvovaginalcandidiasis	Fluconazole 150 mg PO for one dose or topical azoles (e,g, clotrimazole, miconazole) for 3–7 days	Itraconazole 200 mg orally daily for 3–7 days; Boric acid 600 mg vaginal suppository once daily for 14 days for azole refractory candidiasis Severe or recurrent vaginitis: oral fluconazole (100–200 mg) or topical antifungals for ≥7 days	3–7 days

- Take necessary precautions regarding extensive drug interactions among systemic antifungals with ARV and other drugs used for OI management (please refer pertinent data).

- Patients may need hospital admission for supportive care till the oesophageal symptoms improve and necessary long-term treatments are started.

- If diagnosis suggests HSV eosophagitis, use acyclovir 400mg po five times for 14 to 21 days.

PREVENTION

- Administration of ART and immune restoration is an effective means to prevent disease.

- ART failure should be investigated if there is recurrent infection.
- Routine primary prophylaxis is not recommended.
- Secondary prophylaxis or chronic suppressive therapy is not also recommended unless frequent or sever recurrence, if used (Fluconazole 100 mg PO once daily for oral/esophageal and 150 weekly for VVC), discontinue therapy if CD4 count >200 cells/mm3.

PREGNANCY

- Pregnancy upsurges the risk of vaginal colonization with Candida species.
- Topical therapy is preferable for treatment of oral candidiasis in pregnancy, but is essential for vulvovaginal candidiasis, especially during the first trimester.
- Chemoprophylaxis using systemically absorbed azoles against oropharyngeal, esophageal, or vaginal candidiasis should not be initiated during pregnancy or should be discontinued in women who become pregnant.

DIARRHEA

- Diarrhea is among the most frequent symptoms of HIV disease.
- Diarrhea is defined, as passing more than three loose or watery stools per day.
- It may be acute or chronic, persistent or intermittent.
- Diarrhea can result in fluid loss and hemodynamic instability.
- Chronic diarrhea may also lead to nutritional deficiencies and wasting.
- Diarrhea is caused by opportunistic or pathogenic organisms, such as viruses (including HIV), bacteria, protozoa, fungi, helminthic, non-infectious causes and drugs (Diarrhea occurs as an adverse reaction to a number of drugs).
- Risk of a bacterial enteric infections (including bacteremia risk) increases as CD4 count declines, with the greatest risk in patients with CD4 counts <200 cells/mm3.

CLINICAL FEATURES

- Check the duration, volume, frequency, consistency of stools as well as any history of abdominal pain, tenusmus, nausea, vomiting, and presence of constitutional symptoms such as fever.
- Thorough physical examination is necessary to find out the state of hydration and the status of HIV disease.

LABORATORY EVALUATION

- Stool microscopy including modified acid-fast stain.
- Stool culture when indicated (optional in settings with no microbiologic laboratories).

MANAGEMENT

- If specific enteric pathogen is identified by laboratory examination (see table 20) or strongly suspected on clinical grounds, it should be treated accordingly.
- The most important first step is correction of fluid loss. Depending on the severity of dehydration, oral rehydration solution (ORS) or IV fluid therapy can be given.
- Patients with severe dehydration need to be admitted for intravenous fluid administration.
- In children, zinc 20mg per day for 10-14 days (10mg per day for infants < 6months of age) should be added

EMPIRIC TREATMENT OF BACTERIAL ENTERIC INFECTIONS

- Pending Diagnostic Studies: For patients with advanced HIV (CD4 count <200 cells/mm3 or concomitant AIDS-defining illnesses) and clinically severe diarrhea (≥6 liquid stools/day or bloody stool and/or accompanying fever or chills); and/or patients with bloody diarrhea but repeatedly negative stool results especially with constitutional symptoms such as fever.

First line

- ○ **Ciprofloxacin** 500–750 mg PO (or 400 mg IV) every 12 hour

Alternative

- ○ **Ceftriaxone** IV 1 g every 24 hour, or Cefotaxime IV 1g every 8 hour.

NB: Diagnostic fecal specimens should be obtained prior to empiric antimicrobial therapy initiation; and antibiotic susceptibilities should be performed in settings where microbiologic facilities are available to confirm and inform antibiotic choice given increased reports of antibiotic resistance.

- The treatment duration depends on the expected pathogen and may generally extend from 7–14 days for uncomplicated cases and 2 to 3 weeks for complicated (bacteremia, recurrent infection and/or advanced AIDS)
- Hospitalize and use IV antibiotic therapy if marked nauseas, vomiting, diarrhea, electrolyte abnormalities, acidosis, blood pressure instability, and/or when there is a clinical judgment for severity of disease
- For patients with persistent diarrhea (>14 days) but no other severe clinical signs (e.g., dehydration, blood in stool), antibiotic therapy can be withheld until a diagnosis is confirmed.
- Prophylactic antimicrobial to prevent bacterial enteric illness is not usually recommended, including for travelers.
- (Refer to the infectious diarrhea management section elsewhere in this guideline and other pertinent guidelines for management of dehydration).

Table 8.24: Treatment of specific enteric pathogens (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Agent	CD4	Symptom	Diagnosis	Rx
E. hystolytica	any	Bloody stool, colitis	Stool microscopy	Metronidazole
Giardia	any	Watery diarrhea	Stool microscopy	Metronidazole

Cryptosporidium	<150	Watery diarrhea	Modified AFB	ART*
Isospora belli	<100	Watery diarrhea	Modified AFB	TMP-SMX
Microsporidium	< 50	Watery diarrhea	Giemsa stain	Albendazole
CMV	<50	Watery/ bloody diarrhea, colitis	Tissue biopsy	Ganciclovir

**No specific treatment for Cryptosporidium but it will improve with immune restoration following ART.*

SUPPORTIVE TREATMENT

- In adults use anti-diarrheal agents Loperamide 4mg stat then 2mg after each bowel motion or Diphenoxylate 5mg QID. Necessary caution should be taken to avoid anti- motility agents in bacterial or parasitic infectious colitis or enteritis, since toxic mega colon may occur.
- Proper nutritional assessment and support are helpful since patients with chronic diarrhea will develop nutritional deficiencies of variable severity.

PREVENTIVE MEASURES

- Ingestion of contaminated food or water and fecal-oral exposures are most common causes of enteric infections. The risk of infection increases as the CD4 counts declines.
- Hand hygiene: frequently washing hand with soap and water or alcohol-based hand rub.
    - Soap and water are preferred over alcohol-based cleansers, which do not kill C. difficile spores and are only partially active against norovirus and Cryptosporidium.
    - Advised to wash hands after potential contact with human feces (e.g.,

as through defecation, cleaning feces from infants, or contact with a person who has diarrhea), after handling pets or other animals, after gardening or other contact with soil, before preparing food and eating, and before and after sex.

- HIV-infected patients should avoid unprotected sex practices, that could result in oral exposure to feces and, in addition to handwashing.

PERI-ANAL PROBLEMS

- A number of chronic or acute peri-anal problems commonly occur among PLHIV disease, particularly in advanced immunodeficiency.
- These include recurrent peri-anal abscesses, chronic peri-anal fistula, peri-anal herpes (severe, persistent and extensive), and peri-anal warts (sometimes large with obstructive problems).
- Patients with peri-anal problems frequently go to local healers and come with complicated situations.

TREATMENT OF PERI-ANAL ABSCESS IN ADOLESCENTS AND ADULTS

- It is not difficult to make the clinical diagnosis of peri-anal abscess.
- All suspected patients must be thoroughly evaluated and per rectum examination should be done routinely.
- Early treatment is mandatory to avoid extension to peri-anal abscess depending on immunological status of patient and thus more serious morbidity.
- If surgical incision required, it should be done promptly on first visit, or referral made if the surgery is unavailable.
- Otherwise, broad spectrum antibiotics such as amoxicillin-clavulanic acid or alternatively amoxicillin or ampicillin must be administered in sufficient dose for at least 10 days.
- Palliative care including Sithz baths and analgesics are also important.

PERI-ANAL AND/OR GENITAL HERPES

- Latent or active infection with HSV I and II are common in the general population, and is usually mild in immune-competent persons.
- Severe cutaneous disease or visceral involvement is usually restricted to patients with advanced immunosuppression with a CD4 count <100 cell/ mm^3.
- The lesions become extensive, persistent, severe and sometimes with bleeding.
- Unless thorough evaluation with regular inspection of genital and peri-anal areas is done, patients very often don't complain about genital lesions.
- The response to Acyclovir is gratifying if it is done in sufficient dose (400mg 4-5 time/day) and sufficient duration (10 days to 2 weeks in moderately severe or severe cases).
- There is risk of recurrence with severe immunodeficiency. In such cases repeat treatment and put patient on chronic HIV care including ART.
- Herpetic oro-labial infection is treated the same way as ano-genital herpes.
- The treatment of anal and genital warts is particularly frustrating when they are large.
- Unlike other OIs, the response to ART is not satisfactory and the patient continues to suffer despite immunologic recovery.
- Depending on the size, cauterization, podophyllin treatment and surgical debulking, etc. may be tried and patients should be referred to where these services are available.

SEXUALLY TRANSMITTED INFECTIONS (STIS) AND CERVICAL CANCER

- Epidemiological synergy between HIV and STIs is well established, and they frequently coexist.
- Most of these infections are asymptomatic, especially among women.
- However, even asymptomatic STIs can cause complications, transmitted to

sexual partners and enhance HIV transmission.

- STI services should be an important part of comprehensive HIV care among adults and adolescents. Refer the revised STI guideline for syndromic management of STIs

CERVICAL CANCER

- Cervical cancer is a preventable disease and is curable if diagnosed and treated early.
- Women living with HIV have a higher risk of pre-cancerous lesions and invasive cervical cancer.
- Risk and persistence of HPV infection increase with low CD4 count and high HIV viral load.

CERVICAL CANCER SCREENING

- Leads to early detection of precancerous and cancerous cervical lesions that will prevent serious morbidity and mortality, associated with HPV.
- All women with HIV should therefore be screened for cervical cancer. (Refer to guideline for cervical cancer prevention and control in Ethiopia, 2015 or latest).

HCV/HIV CO-INFECTION MANAGEMENT

- HIV patients are among high-risk groups for HCV and should be given priority for screening.
- All HIV patients should be screened and confirmation viral load (VL) test should be done for HCV screened positives.
- Anti-HCV rapid diagnostic test (RDT) or immunoassay (IA) can be used for screening and HCV RNA viral load test using either quantitative or qualitative PCR should be used to confirm chronic HCV infection.
- All chronic HCV infected individuals should be treated to eradicate the virus and achieve cure so that complications can be avoided.
- Follow up quantitative or qualitative HCV RNA viral load is required to confirm if the patient has achieved Sustained Virologic Response (SVR). This should be performed 12 weeks after the completion of therapy.

MANAGEMENT

- Treatment of HCV in HIV infected individuals is not different from non-HIV infected or HCV mono-infected.
- All combination of direct acting antiviral (DAA) including SOF/ LDV, SOF/ RIB and SOF/DCV can safely be used.
- However, attention should be given to drug-drug interactions and shared side effects like head ache, fatigue and anemia.
- According to the viral hepatitis prevention and control guideline, the following are treatment cited options (consult national viral hepatitis prevention and control guideline):
    - **Sofosbuvir** 400 mg oral once daily + **Daclatasvir** 60mg oral once daily for 12 weeks (dose of DCV be adjusted to 90 mg with Efavirenz and 30 mg with Atazanavir/r)
    - **Sofosbuvir** 400mg oral once daily + **Ledipasvir** 90mg oral once daily for 12 weeks.
    - For cirrhotic patient duration will be extended to 24 weeks for above treatment options.
    - **Sofosbuvir** 400mg oral once daily + **Ribavirin** 1000mg (weight < 75kg), 1200mg (weight ≥ 75Kg) twice on divided doses for 24 weeks.
- It is recommended to thoroughly evaluate Chronic HCV infected person with cirrhosis and treatment duration be decided according to the genotype, type of drug selected and addition of ribavirin.

HBV/ HIV CO-INFECTION MANAGEMENT

- HIV co-infection profoundly affects almost every aspect of HBV infection and includes more rapid progression to cirrhosis and hepatocellular carcinoma (HCC), higher liver-related mortality, and decreased treatment response compared with persons without HIV co-infection
- HIV/HBV-co-infected persons also demonstrated rapid HIV disease progression compared to HIV-infected alone, and had an impaired recovery of CD4 cells.

- HIV patients are among the high-risk groups for HBV and should be given priority for screening. i.e., all HIV patients should get screened for HBV and evaluated for chronic infection as per the national viral hepatitis prevention and control guideline.
- After test result, vaccination or treatment and care for reactive patients are recommended when resources permit.

TREATMENT OPTIONS FOR PATIENTS WITH HIV–HBV CO-INFECTION:

- ART should be initiated in all HIV patients regardless of WHO staging or CD4count in individuals co-infected with HIV and HBV with evidence of severe chronic liver disease.
- Combination ART should be initiated with oral drugs containing TDF+3TC (or FTC) as a backbone whenever there is no contraindication (i.e., TDF+3TC + EFV is a preferred regimen).
- Use of lamivudine as mono-therapy in any of these diseases is contraindicated due to high YMDD resistance.
- When switching treatment in patients with HIV on ART failure, the regimen that will continue should have two of the drugs having activity against HBV.
- If tenofovir-associated renal toxicity occurs, the dose of tenofovir should be adjusted according to the renal clearance.

NB: Patients on treatment for HBV and HIV should receive therapy indefinitely. For further reference please consult the national Viral Hepatitis prevention and control guidelines

PREVENTION:

- Vaccination

NERVOUS SYSTEM OPPORTUNISTIC DISEASES

- Neurological manifestations of HIV can occur at any time from viral acquisition to the late stages of AIDS.
- They are varied and may affect any part of the nervous system including the brain, spinal cord, autonomous nervous system and the peripheral nerves.

- HIV affects the nervous system in 70-80% of infected patients due to direct effect of the virus, OIs and/or malignancies.
- For certain neurological manifestations, a single etiology is responsible while in others it is due to multiple causes.
- Most life-threatening neurological complications of HIV occur during the severe immunodeficiency state
- Specific etiological diagnosis in the Ethiopian setting is often a major challenge.
- Neurological complications in HIV patients may be due to:
    - HIV (HIV encephalopathy)
    - OIs (toxoplasmosis, cryptococcal meningitis)
    - Neurosyphilis
    - Malignancies (primary CNS lymphoma); and
    - Drugs (e.g., EFV, etc.)

DIAGNOSIS OF NEUROLOGICAL DISORDERS IN HIV

- Depends on the history and standard neurological examinations.
- There can be single or multiple abnormal neurological findings in the same patient necessitating holistic neurological evaluation.
- Thus, the examination should include assessment of:
    - Mental status comprising cognitive function, orientation and memory.
    - Cranial nerves.
    - Motor function including deep tendon reflexes (DTR).
    - Sensation.

TOXOPLASMA GONDII ENCEPHALITIS

- Toxoplasmic encephalitis (TE) is caused by the protozoan Toxoplasma gondii.

- Disease appears to occur almost exclusively because of reactivation of latent tissue cysts in individuals with underlying immunodeficiency.
- Primary infection occasionally is associated with acute cerebral or disseminated disease.
- Sero-prevalence varies substantially in different communities; in Ethiopia, general prevalence is about 80%.

CLINICAL MANIFESTATIONS

- Among patients with AIDS, the most common clinical presentation of T. gondii infection is focal encephalitis with headache, confusion, fever and/or signs of focal neurological deficit (motor weakness).
- Patients may also present with non-focal manifestations, including only non-specific headache and psychiatric symptoms.
- Focal neurological abnormalities may be present on physical examination, and in the absence of treatment, disease progression results in seizures, stupor, and coma.

INVESTIGATIONS AND DIAGNOSIS

- **Serologic test:** HIV-infected patients with TE are almost uniformly seropositive for anti-toxoplasma immunoglobulin G (IgG) antibodies. The absence of IgG antibody makes a diagnosis of toxoplasmosis unlikely but not impossible. On the other hand, positive test or high titer for Ig-M would suggest a more recent infection. Anti-toxoplasma immunoglobulin M (IgM) antibodies usually are absent. Quantitative antibody titres are not useful for diagnosis.

NEURO-IMAGING (CT SCAN OR MRI OF THE BRAIN)

- Definitive diagnosis of CNS toxoplasmosis requires a compatible clinical syndrome; identification of one or more mass lesions by CT, MRI, or other radiographic testing; and detection of the organism in a clinical sample.
- In the absence of imaging support, empirical treatment is justified when patients present with focal neurological findings and the CD4 count is < 200 cells **µl**.

- Failure to respond to conventional therapy, based on presumptive clinical diagnosis within a week or two of initiation of therapy, suggests the diagnosis to be unlikely.
    - With empirical treatment for toxoplasmosis, nearly 90% of patients will demonstrate clinical improvement within days of starting therapy.
    - Radiological evidence of improvement is usual after 14 days of treatment.

TREATMENT OBJECTIVES

- Prevent or minimize neurologic sequelae

First line regimen for TE in the Ethiopian context is:

- Trimethoprim/sulfamethoxazole 80/400, oral, 4 tablets 12 hourly for 28 days, followed by 2 tablets 12 hourly for 3 months in adults.
- In children 10mg of trimethoprim + 50mg of sulfamethoxazole/kg per dose every 12 hours for 28 days followed by maintenance therapy at 50% reduced dosage for three months.

Alternative regimen

- Sulfadiazine, 1-2 gm PO QID for six weeks or 3 weeks after resolution of lesion PLUS Pyrimethamine: loading dose of 200 mg once, followed by 50-75 mg/day for six weeks. PLUS Folinic acid (Leucovorin): 10-20 mg/d for six weeks OR
- Pyrimethamine and Folinic Acid (Leucovorin): (standard dose) PLUS Clindamycin: initially 200-400mg I.V. then 600 mg QID (300-900mg) OR
- Sulfadoxin Pyrimethamine, 1000mg/50mg, P.O., BID for two days, and then one tablet/day for 6 weeks. PLUS, Folinic Acid (Leucovorin): (standard dose) for 6 weeks
- Followed by Maintenance treatment with Pyrimethamine, 25mg/day P.O., QD

CHRONIC MAINTENANCE TREATMENT (SECONDARY PROPHYLAXIS) FOR TE:

- Co-trimoxazole 960mg daily for adults.
- Discontinuing chronic maintenance therapy if: successfully completed initial therapy, remain asymptomatic of signs and symptoms of TE, and CD4 count >200 cells/mm3 for >6 months in response to ART.
- Reinitiate prophylaxis if CD4 count <200 cells/mm3

SIDE EFFECTS OF DRUGS

- **Sulfadiazine**: crystal urea, rash; Contraindication: severe liver, renal and hematological disorders; known hypersensitivity to Sulphonamides.
- **Pyrimethamine**: rash, fever and bone marrow suppression (neutropenia and thrombocytopenia). Contraindication: folate deficiency
- **Clindamycin**:fever,rash,nausea and diarrhea (including pseudomembranous colitis or diarrhea related to Clostridium difficile toxin).

OTHER SUPPORTIVE MEASURES

- Adjunctive corticosteroids should be used for patients with radiographic evidence of midline shift, signs of critically elevated intracranial pressure and altered sensorium or clinical deterioration within the first 48 hours of therapy.
    - Dexamethasone 4 mg every six hours (0.15mg/kg/ dose every 6 hours for children) is usually chosen and is generally tapered over several days and discontinued as soon as possible.
- Anticonvulsants should be administered to patients with a history of seizures and continued at least through the period of acute treatment, but should not be given for prophylaxis to all patients with the presumed diagnosis of TE.
- Careful attention needs to be paid to any potential drug interactions.

PRIMARY PROPHYLAXIS

- Aimed at preventing 1st Episode of Toxoplasma gondii Encephalitis
- First line: Sulphamethoxazole-Trimethoprim, 60/800mg P.O., Q24 hours (TMP-SMX 1 DS PO daily)

- Indications for Initiating Primary Prophylaxis:
    - o Toxoplasma IgG positive patients with CD4 count <100 cells/mm3
- When to discontinuing primary prophylaxis:
    - o CD4 count >200 cells/mm3 for >3 months in response to ART
- Indication for restarting primary prophylaxis:
    - o CD4 count <100 to 200 cells/mm3 (AIII)

PREGNANCY CONSIDERATIONS

- Pyrimethamine and sulfadiazine are considered safe in pregnancy.
- Pyrimethamine should better be avoided during the first trimester and sulfa drugs (including Sulphamethoxazole, sulfadiazine) have a potential risk of neonatal kernicterus upon exposures in late pregnancy though no clearly convincing data yet.
- The use of TMP (TMP-SMX) in the first trimester should also be evaluated against the potential risk.

CRYPTOCOCCAL INFECTION

- Cryptococcal meningitis is particularly common in advanced immunodeficiency (CD4 count generally <100/mm3).
- It is a major contributor to high mortality before and after ART is initiated because of delayed presentation, together with poor availability and high cost of its treatment.
- Most HIV-associated cryptococcal infections are caused by Cryptococcus neoformans.
- Long-term steroid therapy, as well as other immunosuppressive medicines, is also risks for cryptococal infection.
- Typically, infection is acquired by inhalation of the fungus into the lungs.
- Cryptococcus is found in most warm climate, and is not restricted to the tropics.

PREVENTION OF CRYPTOCOCCAL DISEASE IN PLHIV

- According to a pilot study conducted in Ethiopia from June 2015 to July 2016, in 22 high case load facilities in all regions, the proportion of newly enrolled clients with CD4 count < 100 cells/mm3 was 25.88%. In the same study the prevalence of clients screened positive for cryptococcal antigenemia (CrAg) was high (9.9%).
- The use of routine serum or plasma CrAg screening in ART-naive adults followed by pre- emptive antifungal therapy if CrAg screening is positive is recommended to reduce the development of cryptococcal disease. This should be considered prior to ART initiation:
    - Where patients with a CD4 count less than 100 cells/mm3; and
    - Where this population also has a high prevalence (>3%) of cryptococcal antigenemia.
    - The following algorithm or decision-making guide shows how to decide whether a patient needs prophylactic fluconazole treatment to CrAg screening positive and asymptomatic patients with CD4 count less than 100cells/ml.
    - If the prevalence of cryptococcal disease is high in the locality (most likely in our setups), testing at CD4 count less than 200cells/ml may be preferred.
    - If the CrAg test is not available, prophylaxis might be warranted for patients with low CD4 count (<100 to 200cells/ml) in high-risk areas (>3% of cryptococcal antigenemia).

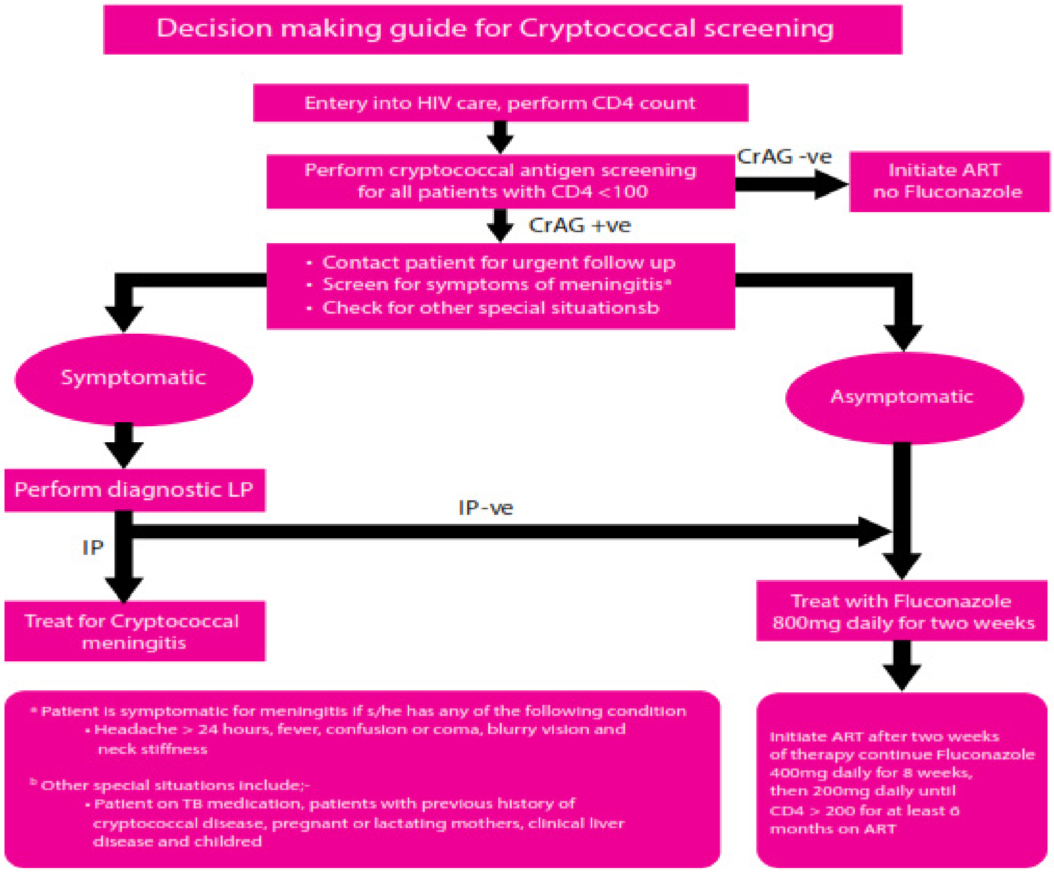
Decision making guide for Cryptococcal screening
Entery into HIV care, perform CD4 count
Perform cryptococcal antigen screening for all patients with CD4 <100
CrAG -ve
Initiate ART no Fluconazole
CrAG +ve
• Contact patient for urgent follow up
• Screen for symptoms of meningitis*
• Check for other special situationsb
Symptomatic
Asymptomatic
Perform diagnostic LP
IP-ve
IP
Treat for Cryptococcal meningitis
Treat with Fluconazole 800mg daily for two weeks
* Patient is symptomatic for meningitis if s/he has any of the following condition
• Headache > 24 hours, fever, confusion or coma, blurry vision and neck stiffness
b Other special situations include;-
• Patient on TB medication, patients with previous history of cryptococcal disease, pregnant or lactating mothers, clinical liver disease and childred
Initiate ART after two weeks of therapy continue Fluconazole 400mg daily for 8 weeks, then 200mg daily until CD4 > 200 for at least 6 months on ART

Figure 8.4: Decision-making guide for Cryptococcus screening (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

TREATMENT OF CRYPTOCOCCI

CLINICAL FEATURES

Sub-acute meningitis, with high mortality:

- In HIV-infected patients, cryptococcosis commonly presents as a sub-acute meningitis or meningoencephalitis with fever, malaise, and headache.
- Headache increasing over days to weeks, nausea, seizures, confusion, irritability, blurred vision, sixth cranial nerve palsy, papilloedema on retinal exam are common.
- Classic meningeal symptoms and signs, such as neck stiffness and

photophobia, occur in only one-quarter to one-third of patients.

- Some patients experience encephalopathic symptoms, such as lethargy, altered mentation, personality changes, and memory loss that are usually a result of increased intracranial pressure, thought to result from impaired CSF absorption, or yeast infection of the brain.
- Coma or a reduced level of consciousness is associated with a poor prognosis.

NON- MENINGEAL PRESENTATIONS OF CRYPTOCOCCOSIS INCLUDE:

- Lung infections: pneumonia or chest pain and cough in a minority of patients, but often no fever.
- Skin lesions and lymphadenitis: Disseminated disease is associated with papular lesions with an umbilicated, centrally depressed area (similar appearance to molluscum contagiosum), which can become ulcerated.

COMPLICATIONS

- Intracranial pressure can become raised (increasing headache, vomiting, and cranial nerve palsy).
- Hydrocephalus, blindness, dementia, and personality change can occur as permanent sequelae.
- Cryptococcomas can develop in the brain, more commonly in patients who are not immunocompromised.
- Coma, cerebral oedema, and death follow if it is untreated, usually due to elevated intracranial pressure.

INVESTIGATIONS AND DIAGNOSIS

- Lumbar puncture (LP) and CSF analysis
    - The opening pressure may be markedly elevated.
    - CSF analysis:
        - Protein: 30-150 mg/dl

  - WBC: 0-100 /mm3 (monocyte)
  - Culture: positive 95-100%
  - Indian ink: positive 60-80%
  - Cryptococcal antigen (Ag) tests > 95 % sensitive and specific
- Serology for cryptococcal antigens: If it is not possible or contraindicated to do LP, serum cryptococcal antigen can be used for diagnosis.
- Chest X ray to demonstrate the organism

MANAGEMENT

- Requires hospitalization and evaluation by physician.
- The treatment is aimed at suppressing fungal growth and preventing squeal related to increased intracranial pressure (ICP).

NON-PHARMACOLOGIC

- Control of raised ICP: daily lumbar puncture with withdrawal of 20-30ml of CSF
- Coma care (including NG tube feeding) if the patient is unconscious

PHARMACOLOGIC

Phases of management: Induction for 2 weeks followed by consolidation for 8 weeks

Table 8.25:Treatment of cryptococcal disease for adults and adolescents living with HIV.

Options	Induction (14 days)	Consolidation (56 days)	Maintenance
Option A	(High dose) Fluconazole 600 mg BID (In children 12mg/kg BID) ± flucytosine 25 mg/kg PO QID	Fluconazole 800 mg/day (children 12mg/kg/day)	Fluconazole 200 mg daily (children 6mg/kg/day) for at least 1 year
Option B	Amphotericin0.7-1 mg/kg/day + fluconazole 800 mg/day OR	Fluconazole 400-800 mg/day or Itraconazole 200 mg PO BID	
	Amphotericin B, 0.7 to 1mg/kg PLUS Flucytosine, 100mg/kg		

If amphotericin used laboratory monitoring and pre-hydration is recommended. N.B. If the patient has meningitis or pneumonia, treatment with a regimen containing amphotericin is preferred provided that facilities allow appropriate monitoring (kidney function and electrolytes).

- Minimize acute infusion reactions when amphotericin is given (e.g., Fever, chills, headache, hypotension) by:
  - Infusing the initial dose slowly over 3–6 hours.
  - Prophylactic antipyretics or hydrocortisone - should only be used in patients who have previously experienced acute infusion reactions (and in whom continued treatment with amphotericin is essential).

MAINTENANCE TREATMENT (OR SECONDARY PROPHYLAXIS)

- Fluconazole 200 mg daily (in children 6mg/kg/day)
- Discontinuation of maintenance treatment (secondary prophylaxis): when patients are stable and adherent to ART and anti-fungal maintenance treatment for at least one year, remains asymptomatic from cryptococcal infection and have a CD4 cell count maintained at greater than or equal to 200 cells/ mm3 (two measurements 6 months apart) or CD4 count ≥100

cells/µL for ≥3 months and suppressed HIV RNA in response to effective ART.

- **Restarting Maintenance Therapy:**
  - If CD4 count declines to ≤100 cells/µL

MANAGEMENT OF ELEVATED INTRACRANIAL PRESSURE (ICP):

- >90% of deaths in the first two weeks and 40% of deaths in weeks 3-10 are due to increased ICP. Thus, it is a must to manage.
- Daily serial LP should be done by drawing 20-30 ml of CSF based on patient's clinical response. Opening pressure should always be measured when a LP is performed.
- Signs of ICP include headache, altered mental status, meningismus and changing in hearing or vision should be closely monitored, if possible opening pressure should be measured.
- There is no role for acetazolamide, mannitol, or corticosteroids to reduce ICP.

TIMING OF ART INITIATION: DELAY INITIATION OF ART

- ART initiation should be deferred until there is evidence of a sustained clinical response to anti-fungal therapy due to life-threatening IRIS risk and
- After 2-4 weeks of induction and consolidation treatment with amphotericin B-containing regimens combined with fluconazole, or
- After 4-6 weeks of induction and consolidation treatment with high-dose oral fluconazole regimen (four weeks with non-meningeal disease).
- NB: Corticosteroids should not be routinely used during induction therapy unless it is used for management of IRIS

POOR PROGNOSTIC SIGNS

- Extra CNS manifestation (especially pulmonary)
- Altered mental status

- Low CSF WBC count, less than 20cells/µL
- High CSF cryptococcal antigen titer

PREGNANCY CONSIDERATIONS

- The diagnosis of cryptococci is similar to the non-pregnant adults.
- Initiate treatment promptly after a diagnosis is confirmed.
- The postpartum period may be a high-risk period for the development of IRIS.
- Lipid formulations of amphotericin B are the preferred initial regimen for the treatment of cryptococcal meningoencephalitis, disseminated disease, or severe pulmonary cryptococcosis in pregnant patients.
- Avoid all triazole agents
- Flucytosine uses do not have human safety data and should not be used unless the benefit outweighs the risk.

NB: watch the drug interactions of azoles with ARV and other drugs for OIs

PERIPHERAL NEUROPATHIES

- Among the most common causes of painful legs in HIV infection (due to complication of HIV infection itself, of drug therapy, or of other metabolic or organ dysfunction or nutritional deficiencies).
- Distal symmetrical sensory polyneuropathy is the most common presentation but mono-neuropathies can also occur.
- The neuropathies associated with HIV can be classified as:
  - Primary, HIV-associated.
  - Secondary causes related to medications (INH), OIs or organ dysfunctions.

DIAGNOSIS

- Peripheral neuropathy diagnosis in HIV-infected patients is based on the clinical picture presenting with pain, tingling sensations, paresthesia or numbness.

- Physical examination can reveal depressed or absent ankle reflex, decreased sensitivity to different modalities of sensation and in severe cases, difficulty in walking.
- The feet and sometimes the hands are involved in symmetrical distribution.
- The diagnosis can be supported by electro-diagnostic studies including electromyography (EMG) and nerve conduction studies (NCS) when available.
- Blood tests are frequently obtained to exclude other causes of neuropathy.
- In most instances, however, diagnosis is almost always clinical.

TREATMENT

- Avoid the offending agent if identified.
- Remove other drugs associated with peripheral neuropathy.
- Supplemental vitamin intake for all patients including concomitant administration of pyridoxine with INH.
- Adjuvants for pain management (such as Amitriptyline, carbamazepine) indicated for patients with pain and paresthesia.

MONITORING OF EVENTS

- Recognize presence of peripheral neuropathy.
- Assess severity at each clinical visit.
- Avoid drugs causing neuropathy.

CUTANEOUS MANIFESTATIONS IN HIV DISEASE

- Early OIs manifestations of HIV infection frequently occurs in the skin.
- Adverse drug reactions (e.g., Nevirapine reactions may be life-threatening) and non-infectious conditions (e.g., neoplasm) or unknown causes also lead to the skin disorders in HIV patients.
- Nevertheless, infections are commonly seen in clinical practice; (Table 8.19)

CLINICAL FEATURES

- **Pruritus** is the most common dermatologic symptom in HIV infected patients.
  - It can be localized indicating primary skin lesion, or generalized that may or may not indicate primary skin lesions.
  - In many patients, pruritus may be severe and may not be amenable to available therapy.
  - The most common skin conditions associated with pruritus in patients with HIV include the following:
    - Excessive dryness of the skin (Xerosis cutis)
    - Eczemas like seborrheic dermatitis or contact dermatitis
    - Folliculitis (may include Staphylococcus aureus infection or hypersensitivity to insects)
    - Drug eruptions
    - Scabies
    - Intertrigo (Candida, tinea, herpes simplex)

DIAGNOSIS

- In most patients, diagnosis of skin disorders with HIV disease can be established by examining the lesions, clinically.
- However, as immune deficiency advances it may be useful to use investigations such as biopsy to diagnose specific dermatosis or use staining and culture to diagnose specific infections.

Table 8.26: Common skin infections in HIV disease (Source: National consolidated Guideline for comprehensive HIV prevention, care and treatment, 2018).

Infections	Disease	Clinical Presentations	Treatment	Remark
Bacterial	Cellulitis	Poorly defined Erythema. Pus and crust at the site plus signs of inflammation.	Amoxicillin 500 mg TID for 14 days or erythromycin 500 mg QID if allergic to penicillin.	Mostly encountered lower extremities and often unilateral.
	Impetigo	Erythematous small papules usually limited to few lesions coalescing in to crusted plaques.	Use topical antibiotics: use Amoxicillin for extensive disease.	Usually a superficial lesion.
	Carbuncle	Nodular Lesion with extensions to the deeper Structure. Signs of Inflammation present.	Use Cloxacillin500mg qid for ten days.	Involves the trunk as well as extremities.

Viral	Herpes simplex	Painful vesicular lesion around mouth or genitalia. Recurrent and extensive, difficult to eradicate during advanced immune deficiency.	Acyclovir 400mg TID for five to ten days. In children 20 mg/ kg/ dose 4X/d; If sever mucocutaneous: acyclovir 5 mg/kg IV every 8 hours, then as above	If Chronic (> one month) patient will benefit from immediate ART initiation if not on ART
	Herpes zoster	Painful and vesicular eruptions with dermatomal distribution. When healed, scar will remain.	Acyclovir 800mg 5X per day for seven days. Monitor renal function.	When it involves the eyes, it is a medical emergency. Do not give Acyclovir* if duration is >72 hours.
	Warts / verrucae	Painless flat to raised warts over fingers or genitalia in advanced immune deficiency, they tend to be multiple and exophytic.	Podophyllin, Imiquimod, Cryotherapy Consult experts	Premalignant and risk for cervical cancer.
	Molluscum Contagiosum	Umbilicated and raised facial lesions that tend to be very big during immunodeficiency state.	May not require therapy;	Contagious

Parasitic infestation	Scabies	Pruritic lesions ranging from pinpointed erythematous papules involving interdigital, axillae and groin areas to varying degrees of hyperkeratotic plaques associated with significant skin thickening and crusting.	BBL, lindane or permethrin to be applied to whole body. Ivermectin 200microgram/kg stat orally.	Burrows are visible in mild infestations but in crust scabies may not be evident leading to misdiagnosis.
Fungus	Dermatophytosis	Superficial causing ringworm or athlete's foot	Topical antifungal for limited skin affected. Fluconazole for extensive lesion 100mg daily for ten days.	
	Thrush	White plaques on the buccal mucosa including the tongues that can be scraped off leaving red base. Can be associated with candida paronychia or intertrigo.	Miconazole gel 2% apply bid Fluconazole 100 mg daily for ten days for recurrent or oropharyngeal thrush.	
	Deep Fungal infection	Presentation varies from fungating nodules and tumors to ulcers and diffuse papulonodular disease	Disseminated Cryptococcus can be confused for Molluscum contagiosum. Treat with amphotericin induction and/ or fluconazole maintenance.	

VARICELLA (CHICKEN POX)

- The varicella virus causes two distinct syndromes in humans:
    - A primary illness called chicken pox, which most often occurs in children and is relatively benign, and
    - A second distinct syndrome called herpes zoster, which occurs in older adults or immunocompromised hosts and is due to reactivation of the dormant virus in the nerves.

CLINICAL FEATURES OF CHICKEN POX

- Prodrome of fever, malaise, nausea, "flu-like" illness. 2–5 days later a generalized, itchy rash appears.
- Crops of papules-vesicles, then crusted lesions appear all over, sparing the palms and soles.
- Lesions co-exist in different stages of progression, i.e. new papules appear when older lesions are already crusted. Intense itching occurs.
- Complications are more often if HIV acquire as adults, and particularly in pregnant.
- Complications may include pneumonia, encephalitis, hepatitis or haemorrhagic syndromes.
- Varicella complications acquired before 28 weeks' gestation, will cause congenital abnormalities in the child (also called congenital varicella syndrome).
- If acquired around the time of birth, it can cause neonatal varicella, which carries a high rate of pneumonia and other complications.

TREATMENT OBJECTIVES

- Prevent complications

Pharmacologic

- In adults including pregnant women:

  - Oral acyclovir, 800mg 5 times daily for 7 days.
- In immunocompromised adults or those with disseminated disease:
  - IV acyclovir 10mg/kg 3 times daily for 7 days; OR high-dose oral acyclovir, if no IV available.
- Start treatment as early as possible ideally in less than 24 hours after symptom onset.
  - For oral treatment, the value of starting after 24 hours is not well established

N.B. The rash can be pruritic and this can be treated with appropriate anti-histamines.

HERPES ZOSTER

- Herpes zoster causes significantly intense and sometimes long-standing pain.
- Herpes zoster in a young person is highly predictive of HIV infection and is a WHO clinical stage 2 conditions.

CLINICAL FEATURES

- Painful vesicular rash in a dermatomal distribution of a nerve supply that does not cross the midline.
  - Pain sometimes comes before the appearance of the rash.
  - Vesicles form in groups and progress to crusted lesions after a few days.
- Most common areas: trunk, particularly the flanks, and forehead.
  - Can involve the eye and cause corneal scarring and blindness.
- HIV patients have more frequent multidermal involvement, involvement of the trigeminal nerve, presence of systemic symptoms, and have a higher risk of disseminated disease.
- Myelitis, meningitis, and encephalitis with headache, fever, neck stiffness, altered motor and sensory function.
- Guillain-Barre syndrome.

COMPLICATIONS

- Blindness due to corneal involvement.
- Post-herpetic neuralgia: chronic pain in the area where the lesions occurred that can last for months to years after the acute episode.

TREATMENT OBJECTIVES

- Prevent post herpetic neuralgia

Non pharmacologic

- Local lesion care with daily bathing with soap and water.
- Isolation of the patient to avoid spreading the virus.
- Avoid contact until all lesions are crusted over.

Pharmacologic

- **Acyclovir 800mg** 5 times daily for 7 days is recommended for all HIV-positive adults. Start acyclovir within 72 hours from the onset of symptoms.
- **Paracetamol** for fever
- **Antihistamines or calamine lotion** may be used to reduce itching
- **Amitriptyline** 25–50mg before bed for neuropathic pain and post-herpetic neuralgia.
- Secondary bacterial infections may require antibiotics.

N.B. For ophthalmic involvement, topical acyclovir, 3% eye ointment applied into the eye every 4 hours should be given.

PRURITIC PAPULAR ERUPTION

- Its prevalence ranges from12-46% and it is uncommon in HIV negatives (PPV of 82-87%, and may play role in diagnosing HIV).

CLINICAL PRESENTATION AND DIAGNOSIS:

- Intensely pruritic, discrete, firm papules with variable stages of development and predilection for extremities, though it can involve trunk and face.

- Excoriation results in pigmentation, scarring and nodules.
- In extreme form, eosinophilia and eosinophilic infiltrates of the skin are present.
- Severity of rash often correlates with CD4 count.

TREATMENT

- Topical steroid and oral antihistamines.
- If refractory (often), short course prednisolone may be used.
- ART is often effective.

VISCERAL LEISHMANIASIS (VL)

(Refer the details under the specific section somewhere in this guideline)

- VL has emerged as a major OI associated with HIV. In HIV patients, VL represents reactivation of latent infection with Leishmania parasite.

CLINICAL FEATURES

- Unexplained fever, splenomegaly & pancytopenia (anemia, leucopenia & thrombocytopenia) are cardinal signs of VL in HIV infected patents. Presentation may not be typical.
- The bone marrow is packed with parasites but two-thirds of cases have no detectable anti Leishmanial antibodies. CD4+ cell count in co-infected patients is usually <300cells/ml.

DIAGNOSIS

- Parasite Detection by microscopic examination of aspirates from lymph nodes, bone marrow or spleen. If available, culture improves the detection of the parasites
- Antibody Detection-DAT and rK39 are extensively evaluated and used for diagnosis of VL.
- Antigen Detection Test- more specific than the antibody-based immunodiagnostic test. A urine latex agglutination (KATEX) has a good specificity but low to moderate sensitivity.

TREATMENT
FIRST LINE

- Liposomal amphotericin B 2–4 mg/kg IV daily (achieve a total cumulative dose of 20–60 mg/kg) or other amphotericin B preparations.

Alternative:

- sodium stibogluconate 20 mg/kg IV or IM daily for 28 days
- Require longer treatment and more liable to relapse.
- Treatment of relapsed patients: is the same as above.

CHRONIC MAINTENANCE THERAPY FOR VISCERAL LEISHMANIASIS

- **Indication**: visceral leishmaniasis and CD4 count <200 cells/mm3
- **First line:** Liposomal amphotericin B 4 mg/kg every 2–4 weeks, or Amphotericin B Lipid Complex 3 mg/kg every 21 days
- **Alternative**: sodium stibogluconate 20 mg/kg IV or IM every 4 weeks

CUTANEOUS LEISHMANIASIS (CL) TREATMENT

First line therapy:

- Liposomal amphotericin B 2–4 mg/kg IV daily for 10 days or interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) to achieve total dose of 20–60 mg/kg, or
- Pentavalent antimony (sodium stibogluconate) 20 mg/kg IV or IM daily for 28 days

Alternative Therapy:

- Oral miltefosine, topical paromomycin, intralesional pentavalent antimony (SSG), or local heat therapy.

CHRONIC MAINTENANCE THERAPY FOR CL

- May be indicated for immunocompromised patients with multiple relapses

PREGNANCY CONSIDERATIONS

- Liposomal amphotericin B is the preferred drug in pregnancy.
- Miltefosine is teratogenic.

PREVENTION

- Reservoir host control in areas with zoonotic transmission and vector control activities, such as indoor residual spraying and/or use of insecticide-treated bed nets.
- Travelers to endemic areas: prevent infection from sand fly bites minimizing nocturnal outdoor activities, wearing protective clothing, and applying insect repellent to exposed skin.
- No chemoprophylaxis

8.3.7 SCREENING FOR CO-MORBIDITIES AMONG HIV PATIENTS

- With the advent of ART, people are living longer; hence they are at risk for age related diseases.
- Therefore, screening of PLHIV for chronic co-morbidities (diabetes mellitus, cardiovascular illnesses, malignancies, chronic liver disease and chronic renal disease) during every visit is a critical component of the care and treatment package.
- WHO has defined a package of essential NCDs (WHO PEN) interventions along with recommendations on screening for and treating of NCD. (https://www.who.int/nmh/publications/essential_ncd_interventions_lr_settings.pdf)

HIV AND MENTAL HEALTH ILLNESSES

- Mental illness has been associated with increased risk for HIV infection, and has been noted to occur at higher rates for HIV- infected individuals.
- Patients with psychiatric symptoms had poor adherence to antiretroviral treatments.

- Treatment of co-morbid psychiatric conditions may improve adherence to ART.
- However, psychiatric conditions were under-recognized and under treated among HIV-infected individuals due to:
  - The overlap between the symptoms of depression and symptoms of HIV disease.
  - The mistaken belief that psychiatric disorders specifically depression and anxiety are usual among HIV patients.
  - The neuropsychiatric side effects associated with some ARVs (ZDV, NVP, ABC, and EFV).

PRIORITY MENTAL HEALTH DISORDERS (BASED ON WHO) INCLUDES

- Psychosis, mania, depression (the most common), suicide, abuse of alcohol and other substances, childhood mental disorders, dementia, and epilepsy should be considered early and treated in PLHIV.
- MOH has developed a National Mental Health Strategy to guide the integration of mental health services into the existing health system.
- ART clinicians can refer difficult cases to psychiatry units within or outside the health facility.

SOURCES:

1. Standard Treatment Guidelines for General Hospitals, 3rd edn. Food, Medicine and Health Care Administration and Control Authority, Addis Ababa, 2014
2. National consolidated Guideline for comprehensive HIV prevention, care and treatment, Ministry of Health, Addis Ababa, 2018

FURTHER READING

3. https://clinicalinfo.hiv.gov/en/guidelines (Accessed December 15, 2020)
4. Ministry of Health-Ethiopia. Implementation manual for DTG rollout and ART optimization in Ethiopia. MOH, Addis Ababa, Ethiopia, 2019

8.4 ACUTE FEBRILE ILLNESSES

8.4.1 OVERVIEW ON ACUTE FEBRILE ILLNESSES

BRIEF DESCRIPTION

- Acute febrile illnesses refer to a large number of diseases in which fever is the major or one of the major clinical presentations.
- Their presentation is acute (within days or less than a day) and patients might visit emergency rooms or general outpatient clinics.
- A wide range of infections can cause acute febrile illnesses.
- The common causes of acute febrile illnesses in a certain area varies depending on a number of factors
  - Geography (high land or low land) and environment
  - The season
  - Whether the setting is in an outbreak/epidemic or non-epidemic setting
  - Patient characteristics: age, comorbidities
- Malaria, upper respiratory tract infections, typhoid fever, and pneumonia are important causes of acute febrile illness.
- Dengue and Chikungunya have emerged as important causes in eastern Ethiopia, in an outbreak/epidemic basis. Yellow fever has also caused significant concern in southern and south west Ethiopia.
- There are a number of misconceptions surrounding acute febrile illnesses among clinicians as well as the public including but not limited to, the followings:
- Investigating patients without fever for acute febrile illnesses
- Investigating patients with just headache or other complaints for acute febrile illness without recording their temperature or in the absence of fever.

- Investigating patients who self-request to be tested for “typhoid” and “typhus” without any history of or recorded fever.
- Relying on unreliable tests
- Serologic tests for typhoid fever and typhus have poor diagnostic accuracy; however they are frequently requested.
- These tests are treated by many clinicians as “diagnostic” tests. This practice is absolutely inappropriate.
- Lack of clinical evaluation (history and physical examination) to identify the possible causes of fever

Examples:

- o Difficulty of swallowing: tonsillitis/pharyngitis
- o Cough, chest pain, shortness of breath: pneumonia
- o Rhinorrhea, nasal congestion sneezing, cough: Viral URTI
- o Ear pain: otitis media
- o Fever and jaundice: malaria, acute viral hepatitis
- o Pelvic pain, vaginal discharge: PID

SPREADING A MISLEADING INFORMATION ABOUT TYPHUS AND TYPHOID TO THE LAY PUBLIC

- By repeatedly testing a patient for “typhus” and “typhoid” and informing them as if they have “a very recurrent” or “a chronic” disease.
- The patients take that information form the clinicians as right information and keep on attributing any illness they develop to typhoid and typhus.

DELAYED DIAGNOSIS OF LIFE-THREATENING FEBRILE ILLNESS

- Due to too much reliance on the serologic tests for typhoid and typhus, many clinicians fail to do appropriate clinical evaluation for life threatening febrile illnesses such as meningitis, severe malaria, and severe sepsis.

EVALUATION OF AN ADULT PATIENT WITH ACUTE FEBRILE ILLNESS

- Assess for life threatening conditions
    - Low BP, hypoxia (desaturation by finger pulse oximeter)
    - Hypoglycemia
    - Confusion
    - Seizure disorder
- Characterize the fever and look for associated (localizing) symptoms and signs: see the algorithm below
- Do appropriate testing (Investigations)
    - CBC
    - Blood film and/or rapid test for malaria
    - Other tests based on clinical suspicion; e.g., chest X-ray if pneumonia is suspected, urinalysis if acute pyelonephritis is suspected, CSF analysis if meningitis is suspected
- Start treatment and follow response closely

ANNEX S: Approach to diagnosis of acute fever in Adults

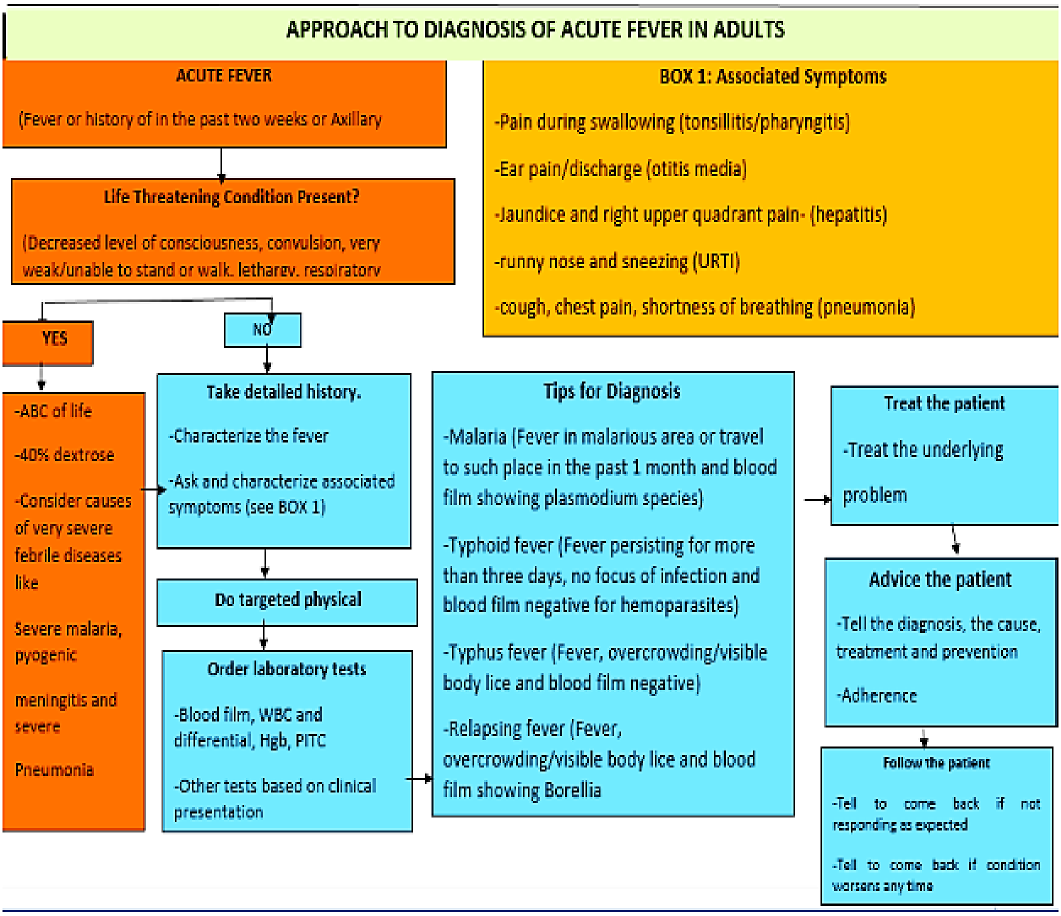
APPROACH TO DIAGNOSIS OF ACUTE FEVER IN ADULTS
ACUTE FEVER
(Fever or history of in the past two weeks or Axillary
Life Threatening Condition Present?
(Decreased level of consciousness, convulsion, very weak/unable to stand or walk, lethargy, respiratory
YES
NO
-ABC of life
-40% dextrose
-Consider causes of very severe febrile diseases like
Severe malaria, pyogenic
meningitis and severe
Pneumonia
Take detailed history.
-Characterize the fever
-Ask and characterize associated symptoms (see BOX 1)
Do targeted physical
Order laboratory tests
-Blood film, WBC and differential, Hgb, PITC
-Other tests based on clinical presentation
BOX 1: Associated Symptoms
-Pain during swallowing (tonsillitis/pharyngitis)
-Ear pain/discharge (otitis media)
-Jaundice and right upper quadrant pain- (hepatitis)
-runny nose and sneezing (URTI)
-cough, chest pain, shortness of breathing (pneumonia)
Tips for Diagnosis
-Malaria (Fever in malarious area or travel to such place in the past 1 month and blood film showing plasmodium species)
-Typhoid fever (Fever persisting for more than three days, no focus of infection and blood film negative for hemoparasites)
-Typhus fever (Fever, overcrowding/visible body lice and blood film negative)
-Relapsing fever (Fever, overcrowding/visible body lice and blood film showing Borellia
Treat the patient
-Treat the underlying problem
Advice the patient
-Tell the diagnosis, the cause, treatment and prevention
-Adherence
Follow the patient
-Tell to come back if not responding as expected
-Tell to come back if condition worsens any time

Fig. 8.5: Approach to diagnose acute fever in adults

8.5 MALARIA

BRIEF DESCRIPTION

- Malaria is a parasitic infection caused by plasmodium species known to affect humans.
- The commonest causes of malaria in Ethiopia are Plasmodium falciparum and Plasmodium vivax. P. falciparum causes virtually all the severe forms of malaria.

- Malaria is a major public health problem in Ethiopia and has been consistently reported as one of the leading causes of morbidity and mortality.
- Prompt diagnosis and treatment is essential in order to prevent complications and death.

CLINICAL FEATURE OF UNCOMPLICATED MALARIA

- Fever, chills, rigors, sweating
- Headache, generalized body and joint pain (myalgia and arthralgia)
- Nausea and/or vomiting, loss of appetite, abdominal pain (especially in children)
- Irritability and refusal to feed (in infants), flu-like symptoms,
- Fever, usually above 38°C
- hepatosplenomegaly
- Pallor

INVESTIGATIONS AND DIAGNOSIS

Investigations

- Microscopy-thick and thin blood films for malaria parasites
- Rapid diagnostic tests (RDT)-if microscopy is unavailable
- CBC

DIAGNOSIS

- The diagnosis of malaria can be confirmed when malaria parasites are demonstrated in the blood films (thick or thin) or with Rapid Diagnostic Test (RDT).
- Blood film is also helpful to estimate the degree of parasitemia, which is very useful not only to predict severity but gauge response to treatment.
- If neither microscopy nor rapid tests are available, diagnosis should be made on the basis of clinical presentation.

- Clinical diagnosis of malaria is made in a patient who has fever or history of fever in the past 48 hours and lives in malaria-endemic areas or has a history of travel within the last 30 days to malaria-endemic areas.
- All patients with malaria should be asked for history of malaria treatment in the past 28 days.

TREATMENT

Objectives

- Decrease individuals morbidity
- Prevent uncomplicated malaria from progressing to severe form
- Improve societal productivity
- Prevent death from malaria complication
- Prevent the development and transmission of drug resistance
- Decrease malaria transmission to others

SUPPORTIVE TREATMENT FOR UNCOMPLICATED MALARIA

- Fever management (axillary temp record of ≥37.50C)
  - o Antipyretics
    - – Paracetamol (acetaminophen) 15 mg/kg (for adults 1000mg) every 4-6 hours, given orally or as a suppository.
  - o Fanning and tepid sponging
- Check for signs of severity
- Assess the ability to tolerate oral medication.
- If there is any sign of severity or the patient is unable to tolerate oral medications admit patients for parenteral treatment.

PHARMACOLOGIC

For uncomplicated (non-severe) malaria: see the table 8.20 and 8.21 for dosing schedules below

- P. falciparum:
  - First line: **Artemether + Lumefantrine** (AL), fixed dose combination (20mg + 120mg) for 3 days + a single dose **primaquine phosphate** (15mg base P.O).
  - First line for pregnant women in the first trimester: quinine
- P. vivax
  - **Chloroquine phosphate** 25 mg/kg given in divided doses over three days
    - 1 g (4 tablets) initially, then 500mg (2tablets) in 6 hours, it is then followed by 500mg (2ablets), PO, daily for 2 days.

      OR

    - 1g (4 tablets) at 0 and 24 hours. It is followed by 500mg (2 tablets) at 48 hrs.
  - **Primaquine phosphate** 15mg base, PO, daily for 14 days for all patients after completing the three days of chloroquine.
- Mixed infections (P. falciparum and P. vivax)
  - Artemisinin based combination therapies (like AL for 3 days) should be used for mixed (falciparum and vivax) infections, followed by 14-day primaquine phosphate.
- Avoid primaquine in pregnant, breast-feeding mothers less than 6 months infants, infants under six months of age.

Table 8.27:Treatment of uncomplicated malaria

Parasite	First line	Alternative
P.vivax	Chloroquine for 3 days + primaquine (PQ) for 14 days	Artemether-lumefantrine/oral quinine + PQ for 14 days
Uncomplicated P.falciparum	Artemether-lumefantrine for3 days + single dose PQ	Other ACTs (3 days) if available or oral quinine + single dose PQ
Uncomplicated mixed infections	Artemether-lumefantrine for 3 days + PQ for 14 days	Other ACTs if available or oral quinine (7 days) + PQ for 14 days

Table 8.28: Dosing schedules of uncomplicated malaria

Tablets containing 20 mg Artemether plus 120 mg Lumefantrine in a fixed dose			
Drug	**Dose**	**Age**	**Weight (KG)**
Artemether-lumefantrine (AL) (Yellow, dispersible pediatric formulation)	1 tab immediately and second 1 tab after 8 hour for the first day, 1 tablet bid for next 2 days	< 4 months	< 5 kg
	1 tab immediately and second 1 tab after 8 hour for the first day, 1 tablet bid for next 2 days	From 4 months to 2 years	5 - 14 kg
AL (Blue dispersible pediatric formulation)	2 tab immediately and second 2 tab after 8 hour for the first day, 2 tablet bid for next 2 days	From 3 years to 7 years	15-24 kg
AL (Brown)	3 tab immediately and second 3 tab after 8 hour for the first day, 3 tablet bid for next 2 days	From 8 years to 10 years	25-34 kg
AL (Green)	4 tab immediately and second 4 tab after 8 hour for the first day, 4 tablet bid for next 2 days	10 years & above	>35 kg

Chloroquine treatment schedule:

Chloroquine is available as tablet (250mg, which is equal to 150mg base) or as syrup (50mg bas per 5 ml). The dose is 25 mg/kg which is given in divided doses over three days

Drug	Dose	Age	Weight (Kg)
Chloroquine phosphate	½ tab on day 1 and ¼ tab on days 2 and 3 OR 5 ml syrup daily on day 1 and 2, and 2.5 ml on day 3	< 4 months	5-6
	½ tab daily for 3 days OR 7.5 ml syrup daily for 2 days and 5 ml for third day	4-11 months	7-10
	1 tab on 1st day and ½ tab daily for next two days OR 12.5 ml syrup daily for 2 days and 7.5 ml for third day	1-2 years	11-14
	1 tab daily for 3 days OR 15 ml syrup daily for 3 days	3-4 years	15-18
	1 ½ tab on day 1 & 2, and 1 tab on third day OR 25 ml syrup daily for 2 days and 15 ml for third day	5-7 years	19-24
	2 ½ tab day 1, 2 tabs day 2, 1 tab on day 3	8-11 years	25-35
	3 tabs on days 1, and 2 tabs daily on second and third days	12-14 years	36-50
	4 tabs on days 1 and 2, and 2 tabs on third day (1g at 0 and 24 hrs followed by 0.5g at 48 hrs PO)	15 years + adults	51+
Primaquine phosphate dose: 0.25 mg base per Kg or 15mg base PO QD for 14 days for adults (administer single dose for P.falciparum or for 14 days for P.vavax)			

Drug	Dose		Age	Weight (Kg)
Primaquine	7.5 mg tablet	15 mg tablet		
	½	-	7 m to 4 years	8-18
	¼	-	5-7 years	19-24
	1	½	8-10 years	25-35
	1 ½	1	11-13 years	36-50
	2	1 ½	14+ years	50+
Oral Quinine dose is 8.3 mg base/Kg (=10mg quinine sulphate salt/Kg) three times daily for seven days. (The max adult dose is 600 mg TID for 7 days)				

Drug	Dosage to be given 3 times daily, orally		Age	Weight (Kg)
Quinine	**200 mg salt**	**300 mg salt**		
	¼	-	2 to 4 months	4-6
	1/3	¼	4 - 12 months	6-10
	½	1/3	1-2 years	10-12
	¾	½	2-3 years	12-14
	¾	½	3-4 years	14-19
	1	¾	5-7 years	20-24
	1 ½	1	8 - 10 years	25-35
	2	1 ½	11 - 13 years	36-50
	3	2	14+	50+

TREATMENT FAILURE

- Consider treatment failure in a patient with malaria who was treated for malaria in the past 28 days.
- The cause might be drug resistance, poor adherence or inadequate drug exposure (i.e. from under-dosing, vomiting, drug interaction, misdiagnosis or substandard medicines.
- If the cause for treatment failure identified early (e.g. anti-malarial drug is vomited), address the cause and reinstituted treatment with the first line anti-malarial drug;
- If a P. falciparum or P. vivax-infected patient returns with fever or history of fever between days 4 to 28 of treatment, microscopic blood examination should be made (do not use RDTs).
    - If parasites are detected, administer second-line drug, e.g., quinine tablets;
    - If blood smear is negative and no other obvious causes found, reevaluate, or refer
- For treatment failure after 28 days, first line antimalarial drugs should be used.

COMPLICATED P. FALCIPARUM MALARIA

- Delayed presentation, delay in diagnosis or inappropriate treatment of uncomplicated malaria can lead to the rapid development of severe or "complicated malaria".
- It is commonly occurring in children under 5 years of age, pregnant women and non-immune individuals. Severe malaria may lead to death unless it is diagnosed early and appropriately managed.

CLINICAL FEATURES

- Inability to take in fluids (or breast milk in children)
- Repetitive vomiting
- Dark or 'cola-colored' urine/ hemoglobinuria

- Passing of very little urine or
- Difficulty in breathing
- Generalized weakness, inability to walk or sit without assistance
- Sleepiness, change of behavior
- Generalized convulsions
- Altered consciousness, confusion, delirium, convulsions, coma
- Circulatory collapse or shock (cold limbs, weak rapid pulse)
- Tachypnea, respiratory distress and/or cyanosis
- Hyperpyrexia (axillary temperature >38.5°C)
- Crepitations/crackles on chest examination
- Spontaneous unexplained heavy bleeding (disseminated intravascular coagulation)
- Hypoglycemia
- Severe anemia (Hb < 6 g/dl) or extreme pallor (severe anemia)
- Acute kidney injury

INVESTIGATIONS AND DIAGNOSIS

Investigations

- Microscopy-thick and thin blood films for malaria parasites
- Rapid diagnostic test (RDT)-if microscopy is unavailable
- Hemoglobin, hematocrit, CBC
- Blood glucose (RBS)
- Blood grouping and cross-matching
- BUN and creatinine
- Lumbar puncture to exclude meningitis or cover with appropriate antibiotic.

DIAGNOSIS

- The diagnosis of severe malaria is based on clinical features and confirmed with laboratory testing. While confirmation of the diagnosis is necessary treatment must be started promptly and not withheld while confirming the diagnosis.

TREATMENT OF SEVERE AND COMPLICATED P. FALCIPARUM MALARIA

Objectives

- Administer medicines parenterally to ensure adequate blood-serum concentrations of the medicine and rapid clearance of parasitemia
- Provide urgent treatment for life threatening problems e.g., convulsions, hypoglycemia, dehydration, renal impairment
- Prevent death from malaria

Non pharmacologic

- Clear and maintain the airway.
- Open IV line for 8 hours of intravenous fluids including diluents for anti-malarial medicine, glucose therapy and blood transfusion.
- Position semi-prone or laterally
- Make rapid clinical assessment.
- Weigh the patient and calculate dosage.
- Exclude or treat hypoglycemia (more so in pregnant women and children).
- Assess state of hydration.
- Measure and monitor urine output.
- If necessary, insert urethral catheter.
- If rectal temperature exceeds 39°C, remove patient's clothes, use tepid sponge,
- Consider other infections.

- Consider need for anticonvulsant treatment

Pharmacologic

- General principles of treatment
  - It is a medical emergency.
  - Parenteral administration required (Artesunate >quinine)
  - Also involves multiple supportive treatment measures

First line

- **Artesunate**, 2.4mg/Kg IV or IM given on admission (time = 0), then repeat at 12 hours, and 24 hours, then once a day for up to 5 days.

OR

- If artesunate is unavailable: **Artemether**, IM 3.2mg/kg loading dose on the first day followed by 1.6mg/kg daily for five days

OR

- If artesunate and artemether are unavailable: **Quinine dihydrochloride:**

Quinine hydrochloride loading dose: 20mg/kg in 500ml of 5% dextrose or normal saline over 4 hours (4ml/minute). The pediatric loading dose is the same but the fluid replacement must be based on body weight.

Maintenance dose: should be given 8 hours after the loading dose at a dose of 10mg /kg and it should be given 8 hourly diluted in 500 ml of 5% dextrose or normal saline over 4 hours

N.B. Give parenteral antimalarials for a minimum of 24 hours, once started (irrespective of the patient's ability to tolerate oral medication earlier)

DOSING GUIDELINES FOR ANTIMALARIAL DRUGS

- Artesunate is dispensed as a powder of Artesunic acid.
- The 60mg vial of artesunate must be reconstituted in two steps:
  - First: sodium bicarbonate solution (Provided separately along with the vial)

- Second: with 5ml of 5% glucose (D5W) solution.
- Full reconstitution results in either 6ml (for intravenous use, with a concentration of 10mg/ml) or 3ml (for intramuscular injection, with a concentration of 20mg/ml).

Table 8.29: Dose Regime of Artesunate IV, IM

Weight (kg) (approximate)	IV 10mg/ml	IM 20mg/ml
0-8	1ml	0.5ml
9 to 12	2ml	1ml
13-16	3ml	1.5ml
17-18	4ml	2ml
19-21	5ml	2.5ml
22-25	6ml	3ml
26-29*	7ml	3.5ml
30-33*	8ml	4ml
34-37*	9ml	4.5ml
38-41*	10ml	5ml
42-46*	11ml	5.5ml
47+*	12ml	6ml

* For persons weighing more than 25 kg, a second artesunate vial must be completely reconstituted as above for each dose, and then each dose administered determined by the chart.

Table 8.30: Dose regimens of Quinine dihydrochloride

Route	Loading dose over 4 hours	Rest for next 8 hours	Maintenance dose over 4 hours (12 hours after start of loading Dose)	Rest for 4 hours	Maintenance dose over 4 hours 8 hourly
IV	20 mg/kg in 500 ml of isotonic saline or 5 % dextrose over 4 hours (4ml/minute)	Give N/Saline or Ringers lactate to keep vein open and maintain fluid balance	10 mg salt/kg body weight in 500 ml of 5 % dextrose over 4 hours	Give N/Saline or Ringers lactate to keep vein open and maintain fluid balance	10 mg salt/kg body weight in 500 ml of 5 % dextrose over 4 hours
IM	**Loading dose**		**Rest for next 4 hours**	**Maintenance dose 8 hourly**	
	20mg/kg body weight divided into 2 site (one in each thigh)			10 mg salt/kg body weight IM into thigh	

The parenteral treatment should be changed to P.O., only after 24 hours and as soon as the patient's condition improves and if there is no vomiting.

- Oral treatment should be given with **Artemether + Lumefantrine** in the doses as indicated above. However, if a patient has a history of intake of **Artemether + Lumefantrine** before complications developed, give **Quinine** tablets 10 mg/kg/dose, TID, to complete 7 days treatment.

SIDE EFFECTS AND OTHER PRECAUTIONS OF ANTIMALARIAL DRUGS

- **Artemether + Lumefantrine (AL):**
  - **Contraindications:**
    - Previous history of reaction after using the medicine
    - Pregnant women in the first trimester
    - Infants less than 5 kg

N.B. Artemether-lumefantrine should not be used as malaria prophylaxis either alone or in combination

  - **Precautions**
    - It should be stored at temperatures below 30°C.
    - It should not be removed from the blister if it is not going to be used immediately.
    - It should preferably be taken with food or fluids; fatty meal or milk improves absorption of the medicine.
- **Artesunate**
  - **Adverse effects**
    - Dizziness, tinnitus, neutropenia, elevated liver enzymes, ECG abnormalities, type I hypersensitivity reaction.
  - **Precautions**
    - The artesunate solution should be prepared for each administration and should not be stored.

- **Artemether**
  - **Adverse effects**
    - Headache, nausea, vomiting, abdominal pain, itching, drug fever, abnormal bleeding and dark urine.
  - **Precautions**
    - IM Artemether should only be used during the first trimester of pregnancy if IV/IM artesunate (preferred) and IV/IM quinine are both unavailable
- **Quinine**
  - **Adverse effects**
    - Cinchonism, including tinnitus, headache, nausea, abdominal pain, rashes, visual disturbances, confusion, blood disorders (including thrombocytopenia and intra-vascular coagulation), arrhythmia, hypoglycemia, and acute renal failure, and hypoglycemia may be caused by quinine
- **Chloroquine phosphate:**
  - **Adverse effects**
    - Gastro-intestinal disturbances, headache, also convulsions, visual disturbances
  - **Precautions: Avoid alcoholic beverages**
  - **Drug interactions:** Carbamazepine, digoxin, ethosuximide, mefloquine, phenytoin and valproic acid.
- **Primaquine**
  - **Adverse** effects: hemolytic anemia, especially in patients with G6PD deficiency;
  - Precautions: In patients with G6PD deficiency; systemic diseases associated with granulocytopenia, e.g., rheumatoid arthritis, and pregnancy and breast feeding).

SUPPORTIVE CARE FOR SEVER MALARIA

- Since death may occur within hours of presentation, supportive care is critical for patients with severe malaria.
- Prompt antimalarial therapy with concurrent supportive care is required to manage life-threatening complications of the disease. This may generally include, check the ABCs in unconscious patients, immediate resuscitative measures, correcting hypoglycemia if present, controlling convulsions, considering the need for blood transfusion and paying attention for body temperature (If >38 °C consider treating it).

FLUID ELECTROLYTE AND ACID BASE DISTURBANCES

Hypovolemia and shock

- Hypovolemia must be assessed on an individual basis.
- Look for: low BP, postural hypotension, low JVP, oliguria, delayed capillary refill.
- Shock: systolic BP <90mmHg or delayed capillary refill with cold extremities
- Start resuscitation measures, if there is evidence of hypovolemia or shock.
- Precautions: patients with severe malaria are more susceptible to fluid overload; there is a narrow threshold between under-hydration and over-hydration (risk of pulmonary and cerebral edema). Hence, close follow up of urine output, respiratory status, and chest auscultation is needed during fluid administration.
    - Management of shock: Intravenous crystalloids (Ringer's lactate or normal saline) 20ml/kg bolus, repeat the IV bolus cautiously if the shock is not persisting after administration of the initial bolus. (See section on sepsis/septic shock for further management)
    - If there is concomitant severe anemia, transfusion is needed.
    - All patients with shock should be evaluated for bacterial septicemia, and empiric IV antibiotics (e.g., ceftriaxone) should be started after sending samples for blood culture (if available).
    - Maintain normal BP, monitor urine output and fluid balance, monitor for signs of pulmonary congestion.

HEMATOLOGIC COMPLICATIONS (INCLUDING SEVERE ANEMIA AND COAGULOPATHY)

- **Anemia:**
  - Indication for transfusion
    - If hematocrit is below 15% (Hg <5g/dl) in a normally hydrated child or adult.
    - Anemia with shock or evidence heart failure, metabolic acidosis (deep labored breathing or high parasitemia (>20% of RBCs parasitized)
  - Volume of transfusion: 10 ml/Kg of packed RBC or 20 ml whole blood/kg of body weight. For adults it is equivalent to 2-3 units of packed RBC or 2-3 units of whole blood.
  - The volume of all blood products should be included in the overall fluid balance. The patient should be closely monitored during the blood transfusion.
- **Bleeding tendency:**
  - Check for evidence of DIC (if laboratory tests are available): platelet count, PT/INR, and PTT
  - Management: Transfusion of platelet and fresh frozen plasma or fresh whole blood (if platelet and fresh frozen plasma are not available).

ACUTE RENAL FAILURE (ACUTE KIDNEY INJURY)

- Persistent oliguria, despite adequate correction of dehydration or hypotension:
  - <17 ml/hour in adults (<200ml in 12 hours or <400ml in 24 hours); < 0.3 ml/kg/hour in children.

    OR
- Elevated serum creatinine: increase in serum creatinine more than twice (two fold) from baseline.

- Management: correct dehydration, if there is any evidence of hypovolemia. Avoid over hydration (fluid overload). If oliguria persists, refer to a facility with dialysis service.

HYPOGLYCEMIA:

- Suspect in any patient who deteriorates suddenly, decreased level of consciousness or convulsions.
- Threshold for intervention among children <5 years is <3 mmol/L (<54 mg/dl); children ≥5 years and adults are <2.2 mmol/L (<40 mg/dl).
- If blood glucose cannot be measured, comatose patients should receive the initial bolus IV dextrose (see below)
- Management
  - IV dextrose: initial bolus
    - 40% dextrose for children: 1ml/kg/dose, diluted with equal volume of NS, give slowly to avoid irritation of vein and extravasation.
    - 40% dextrose for adults: 80ml (4 vials of 20ml preparation) diluted with equal volume of NS, administer slowly.

      OR
    - 10% dextrose (preparation: remove 100ml of fluid from one liter of D5W and add 6 vials (120ml) of 40% dextrose)
    - 10% dextrose for children: 5ml/kg of 10% dextrose bolus
    - 10% dextrose for adults: 300 – 400ml of 10% dextrose
  - Maintain 10% dextrose infusion as maintenance fluid. NG tube feeding should be considered in unconscious patients.
  - Repeat blood glucose measurement every 2-4 hour.

PULMONARY EDEMA AND ADULT RESPIRATORY DISTRESS SYNDROME (ARDS)

- A grave complication of severe malaria associated with high mortality.
- Tachypnea, shortness of breath, hypoxia (low SpO2) crackles on auscultation are common manifestations
- Management:
  - Position patient upright (sitting position)
  - Give oxygen therapy
  - Perform regular suction
  - Stop IV fluids, except for medication administration
  - Give IV diuretics: Furosemide 40 mg IV, if no response increase dose progressively to max 6mg/kg/day
  - Assess the need for intubation & mechanical ventilation.

NEUROLOGIC COMPLICATIONS (INCLUDE ALTERED SENSORIUM, SEIZURE, AND COMA):

- Management of convulsions:
  - Ensure the patient is in a safe environment to avoid injuries
  - Position the patient laterally (sideways) to protect the airways
  - Diazepam
    - Children: 0.15 mg/kg body weight IV or 0.5 mg/kg body rectally
    - Adults: 0.15 mg/kg body weight IV (maximum 10 mg)
    - Watch for signs of respiratory depression; prepare Ambu bag and resuscitation equipment
  - Check for hypoglycemia and correct it.
- **Management of coma**
  - Position the patient on the sides, change positions every 2 hours, correct hypoglycemia and regularly check blood sugar levels.

  - Exclude other causes of coma: like pyogenic meningitis (do LP, unless contraindicated), hepatic failure, renal failure, encephalitis, alcohol (drug) intoxication.

- **Referral**
  - Patients with the following complications need to be referred to a referral hospital
    - Acute kidney injury with indications for dialysis or no improvement in urine output and serum creatinine with conservative therapy: for possible dialysis
    - Respiratory distress or hypoxia not responding to oxygen therapy, diuretics and fluid restriction: for possible mechanical ventilator support.
    - Persistent bleeding diathesis: for transfusion of appropriate blood products (platelets, fresh frozen plasma or cryoprecipitate), if not available.

PREVENTION OF MALARIA

Chemo-prophylaxis

- Persons who travel to malaria-endemic areas are at risk of acquiring malaria.
- Health workers should advise all persons traveling to such areas to avoid mosquito bites, especially by using mosquito repellent and sleeping under long lasting insecticidal nets (LLINs) at night.

First line

- **Mefloquine**, 5mg base per kg weekly (1tablet for adults >50kg, begin ≥ 2weeks before travel to endemic area), take weekly on the same day while in the area and for 4 weeks after leaving the area.

Table 8.31: Dose regimen of Mefloquine as prophylaxis

Weight (Kg)	Age (approx.)	Number of tablets per week
<9	< 3 months	Not recommended
9 – 19	3 – 23 months	¼ tablet
20 – 30	2 – 7 year	½
31 – 45	8 – 10 year	¾
36 – 50+	11 – 14+	1

- **Adverse effects of Mefloquine:** Dizziness, headache, abdominal pain and diarrhea
- **Contraindications:** Persons with known hypersensitivity; persons with a history of severe neurospsychiatric disease; pregnant women in the first trimester; infant less than 3 months; persons performing activities requiring fine coordination and spatial discrimination

ALTERNATIVES

- **Atovaquone/Proguanil:** 250mg/100mg P.O., daily for adults; begin 1-2 days before travel to the endemic area and daily while in the areas and for 7 days after leaving the area.

Table 8.32: Dose regimen of Atovaquone-proguanil chemoprophylaxis

Weight (kg)	Atovaquone/Proguanil HCl Dosage form	Dosage Regimen
11-20	62.5mg/25mg	1 Pediatric Tablet daily
21-30	125mg/50mg	2 Pediatric Tablets as a single dose daily
31-40	187.5mg/75mg	3 Pediatric Tablets as a single dose daily
>40	250mg/100mg (adult tablet)	1 Tablet (adult strength) as a single dose daily

- **Doxycycline: 100mg daily, start** one to two days prior to travel to the endemic area, take daily during the stay, and continue it daily for four weeks following return.
    - o Due to the need for daily intake for more than four weeks, noncompliance is a common problem and an important reason for doxycycline prophylaxis failure when using doxycycline.

SPECIAL POPULATION CONSIDERATIONS

A. **Pregnant women**

- Malaria in pregnancy is associated with premature labor, low birth weight, anemia, and, in low-transmission areas, the risk of severe malaria, and death is high.
- Special consideration for treating pregnant women with malaria
    - o Uncomplicated *P. falciparum* malaria in the first trimester of pregnancy
        - – Avoid: Arthemete Lumfantrene with uncomplicated malaria.
        - – Use: Oral quinine is preferred for patients with first trimester pregnancy.
    - o Uncomplicated P. falciparum malaria or mixed infection in the second and third trimester of pregnancy: treat similarly to non-pregnant patients.
    - o Complicated malaria in all trimester of pregnancy: treat similarly as non-pregnant patients.
    - o Pregnant women with only P. vivax, in all trimesters
        - – Use: chloroquine
        - – Avoid: Primaquine. Primaquine is contraindicated in all trimester of pregnancy and during the first six months of lactation.
        - – Instead of Primaquine: provide chloroquine 2tabs weekly (300mg base/500mg salt), continue during for 6 months of lactation. A full course of Primaquine for 14 days at a dose of 0.25 mg/kg will be given after 6 months of lactation.

- Pregnant women who cannot avoid travel to a malarious area during pregnancy
    - Mefloquine is relatively safe and can be used for prophylaxis
    - Avoid doxycycline.
    - Safety data on atovaquone-proguanil is limited.

A. **Pediatrics:**

- For infants < 5 kg of body weight and with uncomplicated *P. falciparum* malaria: Give Arthemete Lumfantrene (AL) as for children weighing 5 kg.
- Chloroquine is a safe drug that can be used in all children with only P. vivax infection.

FURTHER READING

1. Federal Democratic Republic of Ethiopia Ministry of Health (MOH). MOH National Malaria Guidelines. 4th edn. Addis Ababa, March 2018
2. World Health Organization (2015) Guidelines for treatment of malaria, third edition. Available at http://www.who.int/malaria/en/

8.6 TYPHOID FEVER (ENTERIC FEVER)

BRIEF DESCRIPTION

- Typhoid fever (Enteric fever) is an acute febrile illness characterized by fever and severe systemic illness.
- The causative organism is *Salmonella enterica* serotype Typhi (formerly *S. typhi*).
- Other *Salmonella* serotypes like *S. enterica* serotypes Paratyphi A, B, or C, can cause a similar illness; however, differentiation is not easy but it is not clinically useful.
- Enteric fever is a collective term which refers to both typhoid and parathyphoid fever; however, the term enteric fever and typhoid

- Humans are the only reservoir for *S.* Typhi, the mode of transmission is via contaminated food or water.

Clinical features

- The clinical presentation of typhoid fever can vary from a mild to life threatening in severity.
- Fever is the most important clinical manifestations.
    - For consideration of typhoid fever there must be fever that lasted at least three days
    - The fever characteristically increases daily ("stepwise") reaching as high as in the forties in degree celsius.
- Relative bradycardia (pulse-temperature): normal pulse rate in spite of high-grade fever may be observed.
- Other manifestations: headache, fatigue, malaise, loss of appetite, cough, constipation or mild diarrhea and skin rash or rose spots, hepatosplenomegaly.
- In the late courses of the disease the patient may develop neurologic manifestations
    - "Typhoid encephalopathy": altered consciousness, delirium, and confusion.
    - Acute psychosis
    - Meningeal signs
- Life threatening complications: intestinal perforations, gastrointestinal hemorrhages, and encephalitis.

Table 8.33: Case definitions of typhoid fever

Probable or Suspected case of typhoid fever	A patient with documented fever (38°C and above) for at least 5 days prior to presentation, with rising trend AND Having no other focus to explain the cause of the fever (e.g., malaria, meningitis, pneumonia, abscess, pyelonephritis etc.)
Confirmed case of typhoid fever	A patient with persistent fever (38 °C or above) lasting 3 or more days and S. Typhi isolated on culture (blood, bone marrow culture, stool or urine)
Chronic carrier	An individual excreting S. Typhi in the stool or urine for longer than one year after a blood culture confirmed episode of typhoid fever.

INVESTIGATIONS AND DIAGNOSIS

- The criterion standard for diagnosis of typhoid fever has long been culture isolation of the organism. Cultures are widely considered 100% specific.
- CBC: Usually normal, mild anemia relative leucopenia and occasional thrombocytopenia may be observed
- Liver transaminase and serum bilirubin: usually rise mildly.

DIAGNOSIS

- Microbiologic diagnosis
- The definitive diagnosis of typhoid fever based on culture:
    - Blood culture: the mainstay for the diagnosis
    - Bone marrow culture: has the highest yield
    - Stool or urine cultures
    - Serological tests (Widal test)

  - It is not recommended for diagnosis of typhoid fever.
  - Based on studies done in different parts of Ethiopia the positive predictive value of the Widal test, among febrile patients with suspected typhoid fever is <6%. Hence, a positive or high titer Widal test is by in large a false positive.
- Clinical diagnosis: a patient with documented high-grade fever which is persistent, after exclusion malaria and other causes of fever should be suspected of fever.
- Wrong diagnosis (malpractice)
  - Testing for typhoid fever in patients with non-specific complaints such as headache, malaise, and arthralgia but without high grade fever is malpractice.
  - Diagnosis of typhoid fever based on a positive or high titer Widal test alone in patients without high grade fever is a malpractice.
  - Diagnosis of typhoid fever in patients with high grade fever with Widal test alone without excluding malaria, clinical evaluation and investigation for other cause of fever is malpractice.

TREATMENT OBJECTIVES

- Treat acute infection: decrease morbidty and mortality
- Prevent chronic carriage

Non pharmacologic

Symptomatic treatment:

- Use of antipyretics e.g., paracetamol to control fever, cooling

Pharmacologic treatment

First line

Table 8.34: Drug of choice for complicated and uncomplicated typhoid fever

Drug	First line	Alternative
Uncomplicated Typhoid fever	Ciprofloxacin 500mg P.O., BID for 7 - 10 days	Azithromycin 1 g orally once then 500 mg orally daily OR 1 g orally once daily for 5 to 7 das
Complicated/sever Typhoid fever	Ceftriaxone 2gm IV daily or 1 gm Iv BID OR in 2 divided doses I.M. OR I.V. for 10 to 14 days	Only if no alternative: IV Ciprofloxacin: 20 mg/kg per day in two divided doses (maximum 800 mg per day) then, Oral: 30 mg/kg per day in two divided doses (maximum 1000 mg per day)

ADJUNCT CORTICOSTEROID TREATMENT:

- Indications: Severe systemic illness (delirium, obtundation, stupor, coma, or shock)
- Dexamethasone (3 mg/kg sat, followed by 1 mg/kg every 6 hours for a total of 48 hours)

PREVENTION

- As enteric fever infects from the ingestion of contaminated food or water, sanitation and hygiene, access to clean water and carful consumption of non-cooked/raw foods is critical.
- Typhoid conjugate vaccine for infants and children six months or older is recommended by WHO in endemic areas like Ethiopia.

Special population considerations

- **Pregnant women:** Fluoroquinolone are contraindicated in pregnant mothers. Third generation cephalosporins should be used in pregnant mothers in place of fluoroquinolone or azithromycin.

Referral

- Patients with evidence of peritonitis need emergency surgical intervention. They need to be managed in a setting where there is emergency surgical service.
- Patients with neurologic manifestations should be referred to a tertiary care setting.

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8.7 TYPHUS

Brief descriptions

- Typhus is a febrile illness caused by *rickettisial organisms*.
- The rickettsial fevers (typhus) are acute bacteremic illnesses characterized by fever, headache, rash, confusion in severe cases, meningoencephalitis), in some types, a small black scab or eschar at the site of the insect bite, with local or general lymphadenopathy
- There are two distinct types of typhus:
  - Epidemic typhus:
    - Caused by *Rickettsia prowazekii*

    - Transmitted by a body lice (the feces of the lice)
    - Causes outbreaks/epidemics in unhygienic overcrowded situations
  - Endemic typhus:
    - Caused by Rickettsia typhi
    - Transmitted by the rat flea (inoculation of the feces of the flea)
    - Causes an endemic/sporadic disease.

CLINICAL FEATURES

- The clinical presentation of both types is similar and cause an acute febrile illness characterized by
  - Fever: present in almost 100 % of patients
  - Headache
  - Myalgia and muscle tenderness; which can be severe
  - Rash: begins several days after the onset of symptoms, macular or maculopapular eruption on the trunk and later spreads to the extremities. The rash, usually sparing the palms and soles.
  - Tachypnea
  - Abdominal pain and tenderness
  - Arthralgia
  - Cough
  - Nausea
  - Jaundice
  - Confusion and drowsiness: coma, seizure or development of focal neurologic deficit in some cases.
  - Vasculitis resulting in digital gangrene and cerebral thrombosis are among the more serious complications of typhus.

INVESTIGATION AND DIAGNOSIS

- The diagnosis of typhus is mainly clinical in the appropriate clinical setting.
- Typhus should only be suspected in acutely febrile patient in the right epidemiologic setting.
- Serologic tests are usually negative in the acute setting.
- The gold standard for diagnosis of is indirect immunofluorescence.
- The Weil-Felix:
    - o Has poor sensitivity and specificity.
    - o It should not be ordered in patients without fever, other supportive findings, and appropriate epidemiologic setting.
    - o When there is a strong clinical suspicion: a negative test should not exclude the diagnosis and high titer positive result will not confirm the diagnosis, but it can be used as supportive evidence.
    - o An increasing titer (e.g., a fourfold increase) supports the diagnosis.

OBJECTIVES

- Treating acute infection: decreasing morbidity and mortality

SUPPORTIVE

- Good general care: hydration with follow up of fluid balance, antipyretics and analgesia
- Appropriate antibiotics for secondary infections
- Acute kidney injury: fluid balance, detection and management of complications,

Pharmacologic

First line

- **Doxycycline**, 200mg P.O., in a single or 2 divided doses for 7-10 days

OR

- **Tetracycline**, 250mg, P.O., QID for 7-10 days

Alternatives

- In patients allergic to Tetracyclines, in pregnant women, and in children younger than 8 years of age who require prolonged or repeated courses of therapy
    - **Chloramphenicol (** 500mg P.O., QID for 7 days, for children: 25mg/kg) is the drug of choice.

PREVENTION

- **Epidemic typhus**
    - Delousing
        - Eradication of human lice will prevent spread of the disease.
        - Washing clothes and body
        - Dusting or spraying clothing or bedding: 1% malathion or 1% permethrin
    - **Antibiotic prophylaxis**:
        - A single dose of doxycycline provides protection.
        - For those working or staying in the area a weekly dose should be continued.
- **Endemic typhus**
    - Endemic flea borne typhus can be controlled by anti-rodent measures, and individual use of insect repellent creams.

REFERRAL

- Patients with neurologic manifestation, gangrenes limbs or evidence of venous or arterial thrombosis, severe acute kidney injury should be referred to a referral hospital.

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8 .8 RELAPSING FEVER

BRIEF DESCRIPTIONS

- Louse borne relapsing fever (LBRF or RF) is an acute febrile illness caused by a spirochete, *Borrelia recurrentis*.
- Transmission is confined to the human body louse, *Pediculus humanus corporis*. Infection is by inoculation of louse coelomic fluid or feces by scratching.
- Ethiopia contains endemic foci of LBRF. The disease is common among the homeless and in those living in overcrowded conditions.
- Outbreaks do also occur frequently
- The most distinctive feature of LBRF, the relapse phenomenon, which is characterized by a febrile period (days) alternating with a fever-free period. These febrile-afebrile cycles recur; hence the name relapsing fever.

CLINICAL FEATURES

- **The febrile episode**: starts abruptly with a high-grade fever accompanied by chills and rigors and the following associated with the following clinical features.
    - Generalized aches, arthralgia, back pain,
    - Nightmares

  - Anorexia, nausea, vomiting and diarrhea.
  - Upper abdominal pain
  - Cough
  - Epistaxis
  - Physical findings: tender hepatomegaly, jaundice, petechial or ecchymotic rash (in contrast to the maculopapular rash of typhus), subconjunctival hemorrhages, prostration, confusion, meningismus.
- **The afebrile episode**
  - Untreated febrile episode resolves by crisis after 4-10 (average 5) days, followed by an afebrile period of 5–9 days.
  - Subsequent relapses occur (up to five) often with decreased severity.
- **Poor prognostic features**
  - Shock
  - Coma
  - Myocarditis with acute pulmonary edema
  - Acute respiratory distress syndrome
  - Liver failure; ruptured
  - Bleeding: due to thrombocytopenia or DIC

Spontaneous crisis and Jarisch–Herxheimer reaction (J-HR)

- A massive release of TNF-α which occurs spontaneously or about 1-2 hour following antibiotic administration in patients with RF.
- It is clinically characterized by the following two phases
  - **Chill phase**: It is the initial phase
    - Patient feels an abrupt sense of restlessness and apprehension.
    - A very intense rigors lasting 10 to 30 min
    - Temperature, respiratory rate, pulse rate, and BP rise fast.
    - The fever 9hyperpyrexia could be extremely high
    - Patient becomes delirious.
  - **Flush phase**
    - Characterized by profuse sweating and a slow drop in temprature
    - Falling blood pressure which could be refractory.
    - During this period, patients may collapse and die if they stand up

INVESTIGATIONS AND DIAGNOSIS

Investigations

- CBC: thrombocytopenia is common, leukocytosis or leucopenia can be found.
- Liver enzymes: elevated transaminases, bilirubin or alkaline phosphatase
- Serum creatinine and urea
- ECG: prolongation of QTC, T wave abnormalities or ST depression may be seen in case of myocarditis

- Chest X-ray: normal or evidence of pulmonary edema

DIAGNOSIS

- LBRF should be suspected in a febrile at risk patient.
- Blood film (microscopy):
  - A reliable, quick and cheap bed side diagnostic tool.
  - A thin and a thick blood film must be prepared for Giemsa staining or Wright staining (if Giemsa is not available) should be done.
  - The microscopic diagnosis is fairly straight forward.

TREATMENT

Objectives

- Achievement clearance of spirochetes
- Prevent or minimize the Jarish Herxheimer reaction
- Decrease mortality
- Decrease transmission.

SUPPORTIVE TREATMENT

- Management of spontaneous crisis and J-HR
  - Chills phase: give antipyretics, vigorous fanning and tepid sponging.
  - Flush phase:
    - Patient must stay lying in bed for at least 24 hour.
    - IV crystalloids: with very close follow up of for development of congestion (chest auscultation, JVP, urine output)
  - Evidence of heart failure: Digoxin 1mg stat.

PHARMACOLOGIC (ANTIBIOTIC)

First line

- **P**rocaine penicillin, 400,000-600,000-unit I.M. single dose. For children: 200,000-400,000 units, single dose. Use the lower doses to decrease the risk of J-HR
  - Check blood film after 12 hours of treatment. If negative, give tetracycline 250 mg TID for three consecutive days. If the blood film remains positive, repeat the same dose of procaine penicillin and continue with tetracycline later as described below.
- **Alternatives:** try to avoid these alternatives due to high risk of J-HR unless there is lack of Procaine Penicillin.
  - **Tetracycline** 250- 500mg P.O., single dose. The same dose could be repeated the following day

    OR
  - **Erythromycin,** 500mg P.O., Single dose.

    OR
  - **Doxycycline** 100 -200mg mg, P.O, single dose.

PREVENTION AND CONTROL

- Breaking louse transmission (delousing):
  - Infested clothing should be deloused using heat (>60 °C) or washing with hot water for at least 30 min.
  - Patients should be bathed with soap. Lice have developed some degree of resistance.

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8.9 VIRAL FEBRILE ILLNESSES

8.9.1 CHIKUNGUNYA

BRIEF DESCRIPTION

- Chikungunya is a single-stranded RNA virus that belongs to the family Togaviridae, genus *Alphavirus*.
- The virus is transmitted by bites of infected mosquitoes, largely Aedes aegypti and Aedes albopictus, the same mosquito species which transmit dengue.Transmission by blood products and maternal to child transmission have been reported.
- The first suspected case of chikungunya in Ethiopia was reported in June 2016 from Dolloado district, in the Somalia region.
- The second outbreak in Ethiopia occurred in July 2019 in Dire Dawa town. It affected over 40,000 people.

CLINICAL FEATURES

- Asymptomatic: the infection could remain asymptomatic
- Acute p**hase (first three weeks)**
  - Fever: usually high grade
  - Severe polyarthralgia
    - It is one of the typical features of the disease
    - It can occur with or without definite polyarthritis.
    - Usually involves many joints (ten or more joints), intense and disabling.
    - Bilateral and symmetrical.
    - Involves more distal joints than the proximal ones (hands, wrists and ankles)
  - Myalgia

- Rash
    - Commonly macular and maculopapular rash. There could erythema (diffuse or patchy)
    - Starting from limbs and trunk, can involve the face
    - It can be with or without pruritus
- Facial edema
- Other manifestation: Headache, photophobia
- On physical examination: swelling around the joint areas, joint effusions, lymphadenopathy, and conjunctivitis can be detected.
- Severe complications during the acute phase
    - Not common
    - Occur in the elderly and in those with comorbidities
    - Respiratory failure, myocarditis, acute hepatitis, renal failure, and hemorrhage
    - Neurologic manifestations: meningoencephalitis Guillain-Barré syndrome, transverse myelitis, and cranial nerve palsies, and hearing loss.
    - Ocular manifestations: iridocyclitis, retinitis, episcleritis, macular choroiditis, uveitis)

- **Subacute (post-acute) phase (3 weeks – 3 months)**
    - After a period of some improvement, sometimes without improvement, relapse of signs and symptoms occur.
    - The main manifestations are,
        - Polyarthritis/polyarthralgia: which could be disabling
        - Swelling of the fingers and toes
        - Morning pain and stiffness
        - Carpal tunnel syndrome

- Chronic phase **(more than 3 months**)
    - Some patients develop chronic symptoms
    - The major manifestation of the chronic phase is a chronic polyarthritis which mimic rheumatoid arthritis.

INVESTIGATION AND DIAGNOSIS

Diagnosis

- Chikungunya should be considered in patients with fever and polyarthralgia, in the appropriate epidemiologic setting.
    - 1 to 7 days following onset of symptoms: RT-PCR (reverse transcriptase polymerase chain reaction)
    - ≥8 days following onset of symptoms: antibody testing (IgM and IgG) ELISA or IFA. A positive test establishes the diagnosis.
    - Patients need to be tested for Dengue as well
- Other investigations
    - CBC: thrombocytopenia and lymphopenia are common
    - LFT: raised transaminases may be detected
    - RFT: raised creatinine may be found

TREATMENT

- Acute phase
    - No specific antiviral therapy, management is supportive
    - Rest, fluids, and antipyretics and analgesics
        - Paracetamol: 500 to 1000 mg every 6-8 hours: the preferred agent for fever and joint pain
        - If Dengue is not excluded, avoid NSAIDS.
        - Avoid steroid use in the acute phase.
        - If Dengue is excluded NSAIDS can be used: Ibuprofen 400 to 800 mg TID, Diclofenac 50mg BID to TID.

- Subacute (post-acute) phase
    - NSAIDS for joint pain: Ibuprofen, indomethacin, diclofenac or meloxicam.
    - If pain does not improve or recurs after using NSAIDS: GIVE short course steroid
        - Mild to moderate: Prednisolone 10-20mg for five days, taper to stop in 2weeks.
        - Severe: prednisolone 0.5mg/kg (maximum 40mg), single dose in the morning, after improvement, taper by 5mg weekly.
- Chronic phase
    - Start disease-modifying antirheumatic drug (DMARD) along with the steroid. Taper and stop the treatment
    - Treatment is similar to rheumatoid arthritis
    - First line DMARD: Methotrexate
    - Refer to the details in the rheumatology section

PREVENTION

- Minimizing mosquito exposure is the best method of prevention
- Infected individuals should be protected to avoid mosquito bites during the first week of illness (the likely window of viremia) so as to reduce the risk of local transmission.
- Travelers with risks for severe infection and women late in their pregnancy (as their fetuses are at increased risk), better avoiding travel to areas with ongoing outbreaks.

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8.9.2 DENGUE

BRIEF DESCRIPTION

- Dengue (Dengue fever) is a febrile illness which can range from mild to a life-threatening disease, caused by Dengue viruses.
- Dengue viruses (DENV) are four distinct, single-stranded RNA virus of the genus Flavivirus.
- The four types are designated by numbers as DENV-1, DENV-2, DENV-3, and DENV-4.
- Transmission occurs through the bites of Aedes mosquitoes (Ae. aegypti or Ae. albopictus), the same mosquito species responsible for the transmission of Chikungunya and Zika viruses.
- The likelihood for development of severe dengue is highest among individuals who develop a second dengue fever caused by a different virus type from the initial infection.
- The first outbreak of Dengue in Ethiopia occurred in Dire Dawa city in 2013.
- There was also an outbreak in Somalia region (Kbridhar) in the years 2014 to 2017.

CLINICAL MANIFESTATIONS

- The incubation period of 3–14days (average 7 days)
- The clinical progression follows 3 phases: febrile, critical, and convalescent phases.
    - **Febrile Phase**

  - Lasts 3–7 days
  - Characterized by sudden onset, high-grade fever. Occasionally it could be biphasic (improves and recurs after 1-2days). The following symptoms can be observed
  - Headache, eye pain, joint pain, and myalgia: common.
  - Rash: occurs 2- 5 days after the onset of fever, typically macular or maculopapular
  - Respiratory tract symptoms: cough, sore throat, and nasal congestion.
  - Hemorrhagic manifestations:Variable degree of systemic bleeding may be observed in the

PHYSICAL EXAMINATION FINDINGS IN THE FEBRILE PHASE

- ○ Conjunctival injection, erythematous pharynx, lymphadenopathy, and hepatomegaly.
- ○ Facial puffiness, petechiae and bruising at venipuncture sites).
- ○ A tourniquet test:
  - Inflate a BP cuff on the arm up to a level midway between systolic and diastolic blood pressures for five minutes.
  - Observe the skin of the arm below the cuff: presence of 10 or more new petechiae in one square inch area is considered a positive test.
- ○ **Warning Signs**
  - Warning signs for progression happen in the late febrile phase around time of defervescence. They indicate a high risk of progression to critical phase
  - Severe abdominal pain or tenderness
  - Persistent vomiting

- Mucosal bleeding
- Postural hypotension
- Difficulty breathing, tender hepatomegaly
- Clinical fluid accumulation: pleural effusion ascites
- An increase in hematocrit by more than 20% from baseline with rapid decrease in platelet count
- Lethargy/ restlessness

○ **Critical Phase**

- Begins with defervescence (typically 3-7 days of infection)
- Lasts 24–48 hours
- Characterized by substantial plasma leakage:
- Pleural effusions, ascites, hypoproteinemia, or rising hematocrit.
- Hypotension: may rapidly progress to irreversible shock & death
- Circulatory collapse (dengue shock syndrome): cold skin, weak pulses, capillary refill time greater > 3seconds, reduced urine output and low BP.
- Severe hemorrhagic manifestations can be seen: hematemesis, melena, or menorrhagia.
- Thrombocytopenia
- Uncommon: hepatitis, myocarditis, pancreatitis, and encephalitis.

○ **Convalescent Phase**

- Lasts 2-4 days. Fatigue may persist for days to weeks.
- Plasma leakage subsides, and extravasated fluid starts to be resorbed.
- Pleural effusion ascites decreases and disappear

    - Hemodynamic status stabilizes
    - Diuresis ensues
    - Hematocrit stabilizes or decreases
    - Platelet count increases

INVESTIGATION AND DIAGNOSIS

Diagnosis

- **Clinical diagnosis**
  - A provisional diagnosis should be made clinically in febrile patients with typical clinical manifestations and relevant epidemiological exposure:
    - Fever, headache, myalgia, arthralgia, eye pain, rash, nausea, vomiting rash, hemorrhagic manifestations
    - Positive tourniquet test
    - Leukopenia
- **Laboratory diagnosis**
  - In the first week: RT-PCR (reverse transcriptase polymerase chain reaction) from serum.
  - Serologic diagnosis: can be falsely positive due to cross reactivity with other falvi viruses
    - IgM: A positive result with clinical diagnosis make the diagnosis
    - Paired IgM test: A fourfold or more increase in titer between acute phase test and 10-14 days after the acute phase, confirms the diagnosis
    - IgG: Not useful in the acute phase of the primary infection but can rapidly rise in secondary infections
- **Other investigations**

- CBC: Leukopenia, thrombocytopenia, and increasing hematocrit(hemoconcentration)
- LFT: transaminases are usually elevated.
- RFT: raised serum creatinine and urea may be found

WHO 2009 classification of Dengue

- **Dengue without warning signs**: A presumptive diagnosis of dengue infection may be made in the setting of residence in or travel to an endemic area plus fever and two of the following:
  - Nausea/vomiting
  - Rash
  - Headache, eye pain, muscle ache, or joint pain
  - Leukopenia
  - Positive tourniquet test
- **Dengue with warning signs**: Dengue with warning signs of severe infection includes dengue infection as defined as in Dengue without warning signs + any of the following:
  - Abdominal pain or tenderness
  - Persistent vomiting
  - Clinical fluid accumulation (ascites, pleural effusion)
  - Mucosal bleeding
  - Lethargy or restlessness
  - Hepatomegaly >2 cm
  - Increase in hematocrit concurrent with rapid decrease in platelet count

- **Severe dengue**: Severe dengue infection is defined by the presence of at least one of the following:
    - Severe plasma leakage leading to:
        - Shock
        - Fluid accumulation with respiratory distress
    - Severe bleeding (as evaluated by clinician)
    - Severe organ involvement:
        - Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥1000 units/L
        - Impaired consciousness
        - Organ failure

TREATMENT OBJECTIVES

- Detection and supportive treatment for severe dengue: decrease mortality
- Decrease morbidity

Admission decision

- **Indications for admissions**

Admission criteria for Dengue		
	Presence of warning signs	See above
	Signs and symptoms of hypotension	Clinical signs of dehydration Unable to tolerate oral fluid Postural dizziness Syncope Low BP or cold extremities
	Bleeding	Spontaneous bleeding

	Organ impairment	Renal, liver, neurologic or cardiac • Tender hepatomegaly • Respiratory distress, cyanosis, chest pain
	Investigations	Rising hematocrit
	Co-existing conditions	Pregnancy Old age (>65) or infancy Comorbid conditions: DM, hypertension, obesity, chronic anemias and others
	Social circumstance	Living alone or far from health facility

- **Outpatient management:**
  - For those without any of the admission criteria.

COMPONENTS OF OUTPATIENT MANAGEMENT

- Management of fever:
  - **Paracetamol** 500mg to 100mg every 6-8 hours (maximum 4gm per day)
  - Tepid (barley warm water) sponging
  - Avoid NSAIDS and Aspirin
  - Bed rest
  - Hydration (> 5 glasses of fluid for adults, preferably juice/rice water/soup/milk/ORS than plain
  - Teach warning signs that should prompt to revisit health care facility
  - Bleeding: red spots or patches on the skin, bleeding anywhere

- Frequent vomiting
- Severe abdominal pain
- Drowsiness, mental confusion or seizures
- Pale, cold or clammy hands and feet
- Difficulty in breathing
- To stay under bed net or use insect repellent while febrile
- Identify mosquito breeding site and clear.

- **Inpatient management (see admission criteria): preferably ICU or high dependency area**
  - **Fluid management (see the table below)**

Able to take oral fluids	Warning signs present	Compensated shock: systolic BP maintained but has signs of reduced perfusion)
• Encourage oral fluid intake. • If oral fluid is not tolerated: give NS or RL at maintenance rate • Baseline hematocrit • Monitor vital signs, urine output and clinical status	Obtain baseline hematocrit before fluid therapy. • Normal saline or ringer's lactate ○ Start with 5–7 ml/kg/hr for 1–2 hours ○ Then reduce to 3–5 ml/kg/hr for 2–4 hr, and then ○ Reduce to 2–3 ml/kg/hr or less according to clinical response. • Reassess clinical status and repeat hematocrit: ○ If hematocrit remains the same or rises only minimally: continue with 2–3 ml/kg/hr for another 2–4 hours ○ If hematocrit is rising rapidly and vital signs worsening: increase rate to 5–10 ml/kg/hr for 1–2 hours. • Reassess clinical status, repeat HCT and review fluid infusion rates accordingly • Reduce IV fluids gradually towards the end of the critical phase: indicate by dropping hematocrit and increasing urine output.	Obtain baseline hematocrit before fluid therapy. • Normal saline or ringer's lactate ○ Start with 5–10 ml/kg/hr for 1hr ○ Then reduce to 5-7 ml/kg/hr for 1-2 hr, and then ○ Reduce to 3-5 ml/kg/hr for 2-4hr, then 2-3ml/kg/hr 2-4hr and decrease gradually ○ Total IV fluid: 24-48 hr • Reassess clinical status and repeat hematocrit: ○ If hematocrit remains the same or rises only minimally: Give a bolus of 10-20ml/kg/hr for 1hr ○ If improvement after second bolus: 7-10ml/kg/hr for 1 hr and reduce as above ○ If hematocrit decreasing: blood transfusion. • Reduce IV fluids gradually when the rate of plasma leakage decreases towards the end of the critical phase: indicate by dropping hematocrit and increasing urine output.

Uncompensated shock (hypotensive shock)

- Initiate IV NS or RL 20 ml/kg as a bolus for 15 minutes.
- If patient improves: give 10 ml/kg/hr for 1 hour, then reduce gradually as in compensated shock
- If hematocrit is rising: Give another bolus 10ml/kg/hr for 1 hr
- If hematocrit decreases: transfusion

- **Management of bleeding**
  - Mucosal bleeding may occur in any patient with dengue but, if the patient remains stable, it should be considered as minor.
  - Avoid prophylactic platelet transfusions
  - Avoid intramuscular injections
  - Indications for transfusion
    - Persistent and/or severe overt bleeding with unstable hemodynamic status: regardless of the hematocrit level.
    - Shock with low or normal hematocrit before fluid resuscitation
    - A decrease in hematocrit after fluid resuscitation + unstable hemodynamic status
    - Persistent or worsening metabolic acidosis
  - Give 5–10ml/kg of fresh-packed red cells or 10–20 ml/kg of fresh whole blood
- **Management of fluid overload**
  - Start oxygen therapy
  - Stop IV fluids
  - In the critical phase: do not give diuretics but hold IV fluids or transfusion
  - In the recovery phase: hold Iv fluids, if fluid overload does not improve with spontaneous diuresis, start IV Furosemide 20 -40mg and follow response.

PREVENTION AND CONTROL

- Mosquito control is effective but is difficult to sustain.
- Minimizing mosquito exposure is the best method of prevention
- Infected individuals should take precautions to avoid mosquito bites so as to avoid transmission.
- Travelers should take care to avoid mosquito bites,
- A vaccine, Dengvaxia®, is available in some countries for ages 9-45 years old.WHO recommends it only for individuals with confirmed prior dengue virus infection.

FURTHER READING

1. Centers for Disease Control and Prevention. Dengue Case Management. https://www.cdc.gov/dengue/resources/DENGUE-clinician-guide_508.pdf.
2. World Health Organization. Dengue: Guidelines for diagnosis, treatment, prevention and control, New edition. WHO, Geneva 2009. https://apps.who.int/iris/handle/10665/44188
3. Senanayake A M Kularatne. Dengue fever. BMJ 2015;351:h4661.

8.9.3 YELLOW FEVER (YF)

BRIEF DESCRIPTION

- Yellow fever is a mosquito-borne viral hemorrhagic fever with a high case-fatality rate, in sever conditions.
- The yellow fever virus is an arbovirus of the flavivirus genus. It is transmitted by mosquitoes, belonging to the Aedes and Haemogogus species.
- Different mosquito species live in different habitats: some breed around houses (domestic), others in the jungle (wild), and some in both habitats (semi-domestic). There are 3 types of transmission cycles:
    - ○ Jungle (Sylvatic) yellow fever: In tropical rainforests, monkeys, which are the primary reservoir, are bitten by wild mosquitoes. Occasionally humans working or travelling in the forest are bitten by infected

mosquitoes.

- Urban yellow fever: large epidemics occur in urban areas when infected people bring the virus into heavily populated areas with little or no immunity and the area has high density of Aedes aegypti mosquitoes. Transmission is the from human to human to human.
- Intermediate yellow fever: semi-domestic mosquitoes (breeding both in the wild and around households) infect both monkeys and people. Increased contact between people and infected mosquitoes leads to increased transmission.

ETHIOPIA AND YELLOW FEVER

- Yellow fever outbreaks had occurred in the Western and South-Western areas of Ethiopia between 1959 and 1966.
- Recently there was an outbreak in South Omo Zone (2013), Wolayita Zone (August 2018) and Gurage zone (March 2020).

CLINICAL MANIFESTATIONS

- Infected individual cases might be asymptomatic.
- The incubation period is typically 3–6 days
- The clinical manifestation is characterized by three stages: periods of infection, remission and intoxication consecutively.
  - **Period of infection**:
    - Stays 3- 4 days
    - Fever and other non-specific symptoms like fever malaise, headache, joint pain, backache, myalgia, prostration, nausea, and vomiting.
    - On examination: acutely sick, relative bradycardia , erythematous conjunctivae, tongue with red tip and sides but white coated center, hepatomegaly, leukopenia
  - **Remission**

    - Improvement of fever and symptoms lasting up to 24 to 48 hours.
    - Some patients recover at this phase but others progress in to the third phase
  - **Intoxication**
    - Characterized by jaundice (hepatic dysfunction), renal failure, hemorrhagic symptoms or coagulopathy, confusion, delirium, coma eventually shock and multisystem organ failure.
    - Case-fatality is 30%–60%.

INVESTIGATION AND DIAGNOSIS

- The diagnosis is based on clinical manifestations, travel history and serologic testing or PCR.
- Serology: best if done using enzyme-linked immunosorbent assay (ELISA) for IgM.
- Presumptive diagnosis: IgM antibodies presence in a single sample
- Confirmatory diagnosis: A rise in titer between paired acute and convalescent samples or a fall between early and late convalescent samples.

TREATMENT

- There is no specific antiviral therapy available for yellow fever.
- The treatment of yellow fever consists of supportive care:
- Period of infection: rest, oral hydration, paracetamol, tepid sponging. Avoid NSAIDs.
- Intoxication: hospitalize for supportive care.

PREVENTION

- Vaccination is the primary tool for prevention.
  - Vaccination is contraindicated among immunosuppressed individuals (e.g., HIV infected, transplant recipients

- Preventing mosquito bites: insect repellent use, wearing long-sleeved shirts and pants,
- A person with symptoms of yellow fever, should protect oneself from mosquito bites for a week (5 days) after symptoms begin to prevent spreading to other people.

FURTHER READING

1. Christina L. Gardner and Kate D. Ryman. Yellow Fever: A Reemerging Threat. Clin Lab Med. 2010 March; 30(1): 237–260.
2. Abrham Lilay , Negga Asamene, Abyot Bekel et al. Reemergence of yellow fever in Ethiopia after 50 years, 2013: epidemiological and entomological investigations. BMC Infectious Diseases (2017) 17:343

8.10 PULMONARY INFECTIONS

8.10.1 COMMUNITY ACQUIRED PNEUMONIA (CAP)

BRIEF DESCRIPTION

- Pneumonia refers to acute inflammation of the distal lung-terminal airways, alveolar spaces, and interstitium.
- Pneumonia is a common
- The clinical presentation and the etiology vary greatly depending on the age of the patient, the infecting organism, the site/s the infection has involved, immune status of the patient and the place of acquisition of infection.
- Etiology **of CAP**
    - *Streptococcus pneumonia* is the most common etiology.
    - Others: *Mycoplasma,* Chlamydia, *H. influenzae*, *M. catarrhalis*, *Legionella* (especially in elderly, smokers), *viral* (especially in young) , *Klebsiella* & other gram-negative bacteria (mainly in alcoholics & during aspiration),

S. aureus (especially post-viral infection)

CLINICAL FEATURES

- Although signs, symptoms & imaging do *not* reliably distinguish between "typical" and "atypical" pneumonia, the following can give clues.
- **"Typical"** (*S. pneumonia*, *H. influenzae*)
  - Acute onset of fever, cough with purulent sputum, dyspnea
  - Consolidation on CXR.
- **"Atypical" (***Mycoplasma*, *Chlamydia*, *Legionella*, viral)
  - More insidious onset of dry cough
  - Extrapulmonary symptoms may be present (nausea/vomiting, diarrhea, headache, myalgias, sore throat)
  - Patchy interstitial infiltrates on CXR
  - Elevated transaminases & low serum sodium with *Legionella.*

IDENTIFYING SITE OF CARE

- Although it can't completely replace clinical judgement, clinicians need to use prognostic criteria to decide at the setting of treatment pneumonia (inpatient versus outpatient).
- The CURB-65 is relatively easy to use criteria for this purpose.

Table 8.35: CURB-65 criteria for deciding the setting of treatment in CAP

C	**C**onfusion* (1 point)
U	**U**rea >20 mg/dL (7 mmol/L) ** (1 point)
R	**R**espiratory rate ≥30 breaths per minute (1 point)
B	Low systolic (<90 mmHg) or diastolic (≤60 mmHg) **B**lood pressure (1 point)
65	Age ≥**65** years (1 point)

[*] Defined as an Abbreviated Mental Test Score ≤8 or new disorientation to person, place, or time.

[**]Urea is blood urea nitrogen [BUN], expressed in mg/dL or serum urea concentration, expressed in mmol/L

CURB-65 score	Site of management
0	Outpatient treatment, PO antibiotic
1-2 point	Inpatient management, with IV antibiotics, in a general ward. Those with a score of 1, due age ≥ 65 can be managed as an outpatient.
3 to 5 points	Inpatient management with IV antibiotics; evaluate for ICU admission.

- Indications for ICU admission: ICU admission is required if the patient has severe CAP only. See the table below for criteria defining severe CAP.

Table 8.36: Criteria for defining severe CAP

Major criteria: the presence of one of the following two major criteria

1. Septic shock requiring vasopressor
2. Respiratory failure requiring mechanical ventilation

Minor criteria: three or more of the following (nine) criteria found in a patient

1. Confusion/disorientation
2. Hypotension requiring aggressive fluid resuscitation
3. Respiratory rate ≥ 30 breaths/min
4. Multilobar infiltrates
5. Blood urea nitrogen level ≥20 mg/dl
6. White blood cell count <4,000 cells/ml
7. Platelet count <100,000/ml
8. Hypothermia (core temperature, <36^0 C)
9. PaO2/FI O2 ratio ≤250

INVESTIGATIONS AND DIAGNOSIS

- **Chest X-ray (CXR)**: it is the most important investigation in the diagnosis pneumonia and all patients considered to have pneumonia should have CXR.
- **Sputum gram stain and culture**:
    - It is not routinely recommended for majority patients.
    - In patients with severe pneumonia requiring hospitalization, pretreatment sputum or endotracheal aspirate (if intubated) along with blood culture need to be sent.
    - Patients to be treated empirically for MRSA or P. aeruginosa need also pretreatment sputum gram stain and culture plus blood culture.
- PCR for specific viruses (e.g., SARS COV-2): in the right epidemiologic setting.
- Thoracentesis and pleural fluid analysis
    - Do thoracentesis and pleural fluid analysis, if the size of pleural effusion is >2.5 cm in lateral decubitus position or obvious large (more than ½ of hemithorax), loculated, or with presence of pleural thickening
    - Do pleural fluid: cell count with differential, gram stain and culture, chemistries (glucose, LDH, protein), if there is blood gas analyzer do PH,
- **Other laboratories**
    - CBC with diff
    - In patients with severe pneumonia: BUN/Cr, LFT, serum electrolytes, and blood glucose.

TREATMENT OBJECTIVES

- Achieve clinical cure
- Prevent complications and associated morbidity and mortality.

NON PHARMACOLOGIC

- Bed rest
- Frequent monitoring of all the vital signs in order to detect complications early and to monitor response to therapy, for all patients.
- Give attention to fluid and nutritional replacements as required.
- Administer Oxygen via nasal prongs or face mask (e.g., if saturation <94%)

EMPIRIC ANTIBIOTIC

- Evaluate the patient for the following two parameters before starting empiric antibiotic
  - Look for risk factors include of MRSA (Methicillin Resistant *Staphylococcus aureus)* or P. *aeruginosa*
    - Recent hospitalization
    - Receipt of parenteral antibiotics in the last 90 days
    - Prior isolation of the organisms from the respiratory samples
  - Comorbidities
    - Chronic heart, lung, liver, or renal diseases
    - Diabetes mellitus
    - Alcoholism
    - Malignancy
    - Asplenia
- The duration of antibiotic therapy is generally 5 to 7 days; however, it needs to be guided by clinical response as well. Improvement in vital sign abnormalities (HR, RR, BP, oxygen saturation, and temperature), ability to eat, and normal mentation are needed for hospitalized patients.
- The antibiotic should be continued until the patient achieves stability but for no less than a total of 5 days.

Table 8.37: Empiric antibiotic recommendations for outpatient management of CAP

CAP categories	Etiology	First line	Second line
CAP :outpatient No-comorbidities AND No risk factors*	S.pneumoniae H.influenzae Atypicals	Amoxicillin X 5- 7 days	Doxycycline OR Clarithromycin/Azithromycin
CAP: out patient With comorbidities	Above + beta-lactamase-producing organisms catarrhalis	**Combination therapy** Amoxicillin-clavulanate AND Clarithromycin/ Azithromycin X 5-7 days	**Combination therapy** Cefuroxime or Cefpodoxime AND Clarithromycin/Azithromycin
CAP for hospitalized patients	Gram positive and negative and atypical microorganisms	Ceftriaxone OR cefotaxime IV + Clarithromycin or Azithromycin for 5 to 7 days	Amoxicillin-clavulanate + azithromycin or Clarithromycin
*Risk factors = risk factors for MRSA or P. *aeruginosa* infections (see the text above)			

Table 8.38. Empiric antibiotic recommendations for inpatient management of CAP

CAP category	First line	Second line	Recent Hospitalization and parenteral antibiotics use (in the last 90 days)
CAP: requiring admission to wards Does not have severity signs requiring ICU admission (see table 2 above)	IV Third generation cephalosporin + Macrolide Ceftriaxone OR Cefotaxime PLUS Azithromycin/Clarithromycin	Levofloxacin or Moxifloxacin alone	Take culture and Add coverage for P. aeruginosa*
CAP requiring ICU admission (Severe CAP)	IV Third generation cephalosporin + Macrolide Ceftriaxone OR Cefotaxime PLUS Azithromycin/Clarithromycin	IV Third generation cephalosporin + Levofloxacin/Moxifloxacin	Take culture and and Add coverage for MRSA and P. aeruginosa*
* Options for P.aeruginosa coverage: piperacillin-tazobactam , cefepime , ceftazidime , imipenem, Meropenem * MRSA coverage: Vancomycin			

Table 8.39: Adult dose recommendations for CAP		
Antimicrobial agent	**Adult dose**	**Comments**
Amoxicillin (A)	1000mg PO TID	First line for outpatient with no comorbidities
Amoxicillin-clavulanate (A)	625mg PO TID or 875 mg/125 mg BID, or 2,000 mg/125 mg BID	First line for outpatient with comorbidities
Benzyl penicillin (A)	2-3 million IU I.V. QID	Can be used as an alternative to amoxicillin
Ampicillin-sulbactam	1.5 to 3 g IV QID	Alternative to cephalosporin's in hospitalized patient, also consider for aspiration pneumonia if anaerobic coverage needed
Cefuroxime (Wa)	500mg PO BID	Alternative to Amoxicillin-clavulanate
Cefpodoxime (Wa)	200mg PO BID	Alternative to Amoxicillin-clavulanate
Ceftriaxone (Wa)	1-2 g IV 12 hourly	First line in severe cases with macrolides
Cefotaxime (Wa)	2 g IV 6 hourly	First line in severe cases with macrolides
Clarithromycin (Wa)	500mg PO BID	WHO recommend it over Azithromycin due to safety concerns
Azitromycin (Wa)	500mg PO, first day then 250mg PO, for 4 days	Associated with cardiovascular issues
Doxycycline (A)	100mg PO, BID	Second line for mild to moderate cases

Levofloxacin (Wa)	500-750 mg PO/IV BID	More side effect (including masking TB), thus only used when no alternative, e.g in sever penicillin allergy
Moxifloxacin (Wa)	400 mg PO BID	See above comment for levofloxacin
Cloxacillin	500mg PO QID	Alternative add on for staph
Vancomycin (Wa)	1g IV BID	Reserved only for MRSA suspicion and used only after culture sample taken
Ceftazidime (Wa)	2g IV q6-8h	Reserved only for pseudomonas suspicion and used only after culture sample taken
Cefepime (Wa)	2 g IV 8-12 hourly	See above comments for ceftazidime
Piperacillin + tazobactam (Wa)	2g IV Q8hr	See above comments for ceftazidime
A = access group antibiotics *Wa = watch group antibiotics* *Re= reserve group antibiotics*		

PREVENTION

- Smoking cessation should be encouraged during the initial visit
- Other infection prevention measures

SPECIAL POPULATION CONSIDERATIONS

- Pregnant: Floroquinolones and tetracyclines (if used) are not recommended in pregnancy.
- Elderly: elderly patients are more likely to have an altered/unusual clinical presentation and increased risk of severe disease. Frequent monitoring schedules are recommended for this group of population.

FURTHER READING

1. Joshua P. Metlay, Grant W. Waterer, Ann C. Long et. al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019. DOI: 10.1164/rccm.201908-1581ST

8.10.2 HOSPITAL-ACQUIRED AND VENTILATOR-ASSOCIATED PNEUMONIA

DEFINITIONS

- Hospital-acquired (or healthcare associated) pneumonia (HAP) is pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission.
- Ventilator-associated pneumonia (VAP) is a type of HAP that develops more than 48 hours after endotracheal intubation.
- Healthcare associated pneumonia (HCAP): is no more used currently.
- HCAP is now classified under CAP, with risk factors MDR pathogens, particularly MRSA and *P aeruginosa*.

INVESTIGATION AND DIAGNOSIS

- Clinical diagnosis: Clinical diagnosis of HAP and VAP requires the following three parameters to be present.
    - A new or progressive lung infiltrate on chest X-ray.
    - Clinical evidence to indicate the lung infiltrate is of infectious origin: one or more of the followings
        - A new onset of fever
        - Purulent sputum
        - Leukocytosis/leukopenia
        - Decline in oxygenation.

    - Time of presentation: after 48 hours of admission for HAP and after 48 hours of intubation for VAP.
- Identification of pathogen: Cultures from lower respiratory samples should be taken before initiation of antibiotic.
- Risk factors for increased mortality in HAP
  - Septic shock
  - Requirement for mechanical ventilator support
- Risk factors for Multidrug resistant pathogens in HAP/VAP.
  - Risk factors for MDR VAP:
    - Prior intravenous antibiotic use within 90 days
    - Septic shock at time of VAP
    - ARDS preceding VAP
    - Five or more days of hospitalization prior to the occurrence of VAP
    - Acute dialysis needed prior to VAP onset
  - Risk factors for MDR HAP
    - Prior intravenous antibiotic use within 90 days

EMPIRIC TREATMENT FOR COMMONLY SUSPECTED ETIOLOGIES OF HAP/VAP

- The empiric antibiotic choice for HAP and VAP: needs to consider *Pseudomonas aeruginosa*, other gram-negative bacilli, and *Staphylococcus aureus*.
- Since delayed and inappropriate therapy is associated with high mortality, early and aggressive treatment with early and aggressive de-escalation is an important composite for HAP/VAP (particularly for VAP) management
- If possible, hospitals need to regularly generate and disseminate a local antibiogram, tailored to their HAP population.
- Duration of therapy: a seven days course is generally adequate for both HAP and VAP. A shorter or longer duration can be considered based on clinical response.

Table 8.40: Empiric antibiotics for HAP (not VAP)

Population	Antibiotic choices	Remarks
HAP with one of the following • Septic shock • Requiring mechanical ventilation • Received antibiotic in the last 90 days	A combination of three antibiotics: one from of the following lists • One of the following ○ Cefepime 2 g IV q8h ○ Ceftazidime 2 g IV q8h ○ Meropenem 1 g IV q8h ○ Imipenem 500 mg IV q6hd ○ Piperacillin-tazobactam 4.5 g IV q6h **PLUS** • One of the following ○ Gentamicin 5–7 mg/kg IV q24h ○ Ciprofloxacin 400 mg IV q8h **PLUS** • Vancomycin 15 mg/kg IV q8–12h (for severe cases, loading dose 25–30 mg/kg, maximum 3g)	• Double antipseudomonal coverage + MRSA coverage • Antibiotics need to be deescalated based on culture and sensitivity results, if there is clinical improvement. • Doses need to be adjusted in patients with impaired renal function.

HAP with none of the following • Septic shock • Requiring mechanical ventilation • Received antibiotic in the last 90 day	A combination of two antibiotics • One of the following ○ Ceftazidime 2 g IV q8h ○ Meropenem 1 g IV q8h ○ Imipenem 500 mg IV q6hd ○ Piperacillin-tazobactam 4.5 g IV q6h **PLUS** ○ Vancomycin 15 mg/kg IV q8–12h (for severe cases, loading dose 25–30 mg/kg, maximum 3g)	If the proportion of the unit's *Staphylococcus aureus* isolates thus far has been known to be < 20%, the vancomycin can be omitted and one of the following can be used: ○ Piperacillin-tazobactam 4.5 g IV q6h ○ Cefepime 2 g IV q8h

Table 8.41: Empiric antibiotics for VAP

Population	Antibiotic choices	Remarks
VAP with one of the following risk factors • IV antibiotic use within the previous 90 days • Septic shock at the time of VAP • ARDS preceding VAP • ≥5 days hospitalization prior to the occurrence of VAP • Dialysis prior to VAP onset	A combination of three antibiotics: one from of the following lists • One of the following ○ Cefepime 2 g IV q8h ○ Ceftazidime 2 g IV q8h ○ Meropenem 1 g IV q8h ○ Imipenem 500 mg IV q6hd ○ Piperacillin-tazobactam 4.5 g IV q6h **PLUS** • One of the following ○ Gentamicin 5–7 mg/kg IV q24h ○ Ciprofloxacin 400 mg IV q8h **PLUS** Vancomycin 15 mg/kg IV q8–12h (for severe cases, loading dose 25–30 mg/kg, maximum 3g)	➢ Double antipseudomonal coverage + MRSA coverage • Antibiotics need to be deescalated based on culture and sensitivity results, if there is clinical improvement. . • Doses need to be adjusted in patients with

VAP with none of the above risk factors	A combination of two antibiotics • One of the following ○ Ceftazidime 2 g IV q8h ○ Meropenem 1 g IV q8h ○ Imipenem 500 mg IV q6hd ○ Piperacillin-tazobactam 4.5 g IV q6h **PLUS** Vancomycin 15 mg/kg IV q8–12h (for severe cases, loading dose 25–30 mg/kg, maximum 3g)	If the proportion of the unit's *Staphylococcus aureus* isolates is< 10%, the vancomycin can be omitted and one of the following can be used: ○ Piperacillin tazobactam 4.5 g IV q6h ○ Cefepime 2 g IV q8h

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2. Torres A, Niederman MS, Chastre J, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia. EurRespir J 2017; 50: 1700582 [https://doi.org/10.1183/13993003.00582-2017].

_8.10.3 EMPYEMA AND COMPLICATED PARAPNEUMONIC EFFUSIONS

BRIEF DESCRIPTION

- Parapneumonic effusion is an effusion that forms in the pleural space adjacent to a bacterial pneumonia. Most parapneumonic effusions are small and resolves with appropriate antibiotic therapy. However, if bacteria invade the pleural space, a complicated parapneumonic effusion or empyema develops.

- Parapneumonic effusion is classified in to three clinical categories (uncomplicated parapneumonic effusion, complicated parapneumonic effusion, and empyema). These categories indicate the risk of bad outcome and help to decide management.

Uncomplicated parapneumonic effusion	Complicated parapneumonic effusion	Empyema
An exudative effusion with either of the following characteristics • Small size (1cm in lateral decubitus position), non-loculated: gram stain, culture, glucose level of pleural fluid being unknown **OR** • Moderate size (>1cm but <1/2 of the hemithorax), non loculated: **gram stain and culture confirmed to be negative** and pleural fluid glucose >60mg/dl.	An exudative effusion with **negative pleural fluid culture and gram stain** along with the presence of one of the following: • Large non-loculated (free flowing) pleural effusion involving >1/2 of the hemithorax • Loculated pleural effusion • Pleural effusion with thickened pleura • Pleural fluid glucose <60mg/dl	Refers to invasion of the pleural space by a significant number of bacteria. The presence of either of the following defines empyema • Gross pus **OR** • Positive gram stain or positive culture from pleural fluid.

CLINICAL FEATURES

- The clinical features of parapneumonic effusion are similar to pneumonia. Pleuritic chest pain and prolonged fever are more common in patients who develop complicated parapneumonic effusion or empyema.
- Physical examination: signs of pleural effusion (dullness, decreased or absent air entry, decreased tactile fremitus) will be present.

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of parapneumonic effusion requires chest imaging.
    - Chest X-ray: all patients with suspected pneumonia should have chest X-ray
    - Chest ultrasound: if the chest X-ray shows effusion, proceed to chest ultrasound. The ultrasound helps to detect loculated effusion, differentiate solid mass from effusion.
    - Chest CT-scan: if the ultrasound is inconclusive or suggestive of another diagnosis.
- Thoracentesis is diagnostic): indicated if one of the following is found
    - Loculated
    - Non-loculated (free flowing): size is >1cm in lateral decubitus, moderate or large
    - Associated with thickened parietal pleura
    - Ultrasound guided drainage is preferable particularly to loculated effusion.
- Pleural fluid analysis:
    - Cell count with differential
    - Gram stain and culture
    - Pleural fluid chemistries (protein, LDH, glucose)
    - When the clinical suspicion for other causes of exudative effusion exists

e.g., tuberculosis, malignancy, connective tissue disorder appropriate tests need to be done.

TREATMENT OBJECTIVES

- Achieve complete resolution
- Prevent development of complications

Table 8.42: Management of parapneumonic effusion and empyema

Types	Treatment
Uncomplicated parapneumonic effusion	Antibiotics alone, no drainage
Complicated parapneumonic effusion	Chest tube drainage* (also called tube thoracostomy) + Antibiotics
Empyema	Urgent chest tube drainage* (tube thoracostomy) + antibiotics
**If clinically & radiologically improve and drainage rate fall below <50 ml/day for 2 to 3 days, remove chest tube* **If no improvement: assess antibiotic coverage (re-culturing, reviewing anaerobic and MDR pathogens coverage) and evaluate for the presence undrained loculated pockets.*	

SURGERY (BEYOND CHEST TUBE DRAINAGE):

- Options: thoracoscopic drainage, standard thoracotomy, or open drainage
- Indications: Multiple loculations or lack of improvement with chest tube drainage

EMPIRIC ANTIBIOTIC REGIMEN

- All patients with parapneumonic effusion or empyema need an antibiotic therapy. Antibiotics should be administered promptly (not delayed for sampling or drainage procedures) for better outcome.

- Anaerobic coverage should be maintained irrespective of culture results as anaerobic organisms are difficult to grow.
- The duration of antibiotic should be decided on patient-by-patient basis; mainly based on clinical response. Complete radiologic resolution might take months.

Table 8.43: Empiric antibiotic choice for parapneumonic effusion and empyema

Types of parapneumonic effusion	First line	Alternative	Duration
• **Community-acquired** uncomplicated parapneumonic effusion	ceftriaxone	○ Amoxicillin-clavulanate	
• **Community acquired** ○ Complicated parapneumonic effusion OR ○ Empyema	○ Ceftriaxone PLUS ○ Metronidazole	○ Piperacillin-tazobactam ○ Ampicillin-sulbactam	2-3 wks: complicated parapneumonic effusion 4-6 wks: empyema
• **Hospital-acquired** ○ Uncomplicated parapneumonic effusion	See treatment of hospital acquired pneumonia	See treatment of hospital acquired pneumonia	1 to 2 wks

• **Hospital-acquired** ○ Complicated parapneumonic effusion OR Empyema	Vancomycin + Metronidazole + Cefepime or ceftazidime	○ Vancomycin + piperacillin-tazobactam OR ○ Vancomycin + Meropenem/imipenem ○ If severe penicillin-allergic: vancomycin + metronidazole + ciprofloxacin	2 to 3 weeks for complicated effusion; 4-6 weeks for empyema

FURTHER READING

1. Steve A. Sahn. Diagnosis and Management of Parapneumonic Effusions and Empyema. Clinical Infectious Diseases 2007; 45:1480–6. DOI: 10.1086/522996
2. H. Davies, R. Davies, C. Davies Management of pleural infection in adults: British Thoracic Society pleural disease guideline 2010. Thorax 2010;65(Suppl 2):ii41eii53. doi:10.1136/thx.2010.137000

8.10.4 ASPIRATION PNEUMONIA AND LUNG ABSCESS

8.10.4.1 ASPIRATION PNEUMONIA

BRIEF DESCRIPTION

- Aspiration is a common in healthy individuals, particularly during sleep. The aspiration generally goes unnoticed without any consequences.
- The development of chemical pneumonitis or aspiration pneumonia depends on the volume and content of the aspirate, and the individual's defense.

- Aspiration pneumonitis (chemical pneumonitis) the chemical induced acute lung injury that occurs after aspiration of acidic sterile gastric contents.
- Aspiration pneumonia: refers to the infectious pulmonary pathology that occurs following abnormal entry of fluid or particulate contents into the lower respiratory tract.
- The aspirated fluid can be oropharyngeal secretions, particulate matter, or gastric content.
- Mixed microorganisms (strict anaerobes and facultative anaerobes and aerobes) cause the infectious pathology.
- Left untreated, aspiration pneumonia may complicate to lung abscess, necrotizing pneumonia, empyema, and bronchopleural fistula.
- Major risk factors for aspiration pneumonia
    - Altered consciousness: alcoholism/drug overdose, seizures/head, general anesthesia
    - Neurologic disorder (e.g., stroke, dementia, Parkinson disease, brain tumor, motor neuron disease)
    - Dysphagia due to various reasons (e.g., esophageal stricture, neoplasm etc.)
    - Mechanical disruption of the usual defense barriers (e.g. intubation, bronchoscopy)
    - Other: Protracted vomiting, pharyngeal anesthesia, general debility, recumbent position, glottic insufficiency etc.

CLINICAL FEATURES

- Aspiration pneumonitis:
    - Abrupt onset shortness of breath, cyanosis, diffuse crackles on lung auscultation
    - Low grade fever
    - Chest imaging showing infiltrates mainly involving dependent

pulmonary segments

- Aspiration pneumonia:
    - Similar to other types of pneumonia cough, fever, purulent sputum, and shortness of breath.
    - Patients with anaerobic organisms may have indolent course, evolving over several days or weeks. Chills and rigors are usually absent, and the sputum could be putrid.

INVESTIGATIONS AND DIAGNOSIS

- Aspiration pneumonitis: the diagnosis is mainly clinical. It is based on the presence of risk factors for aspiration and abrupt onset symptoms. Chest X-ray abnormalities will appear after two hours.
- Aspiration pneumonia: clinical features + Chest X-ray:
    - Chest X-ray: infiltrates, necrosis/cavity involving the lower lobes or the superior segments of the lower lobes or posterior segment of the upper lobes.
- Sputum AFB or geneXpert

TREATMENT OBJECTIVE

- Achieve complete resolution of symptoms
- Prevent development of suppurative complications (lung abscess, empyema)

ASPIRATION PNEUMONITIS

- The main stay of treatment is respiratory support (oxygen therapy, aspiration of obstruction fluid, mechanical ventilation if respiratory failure)
- Due to the difficulties in excluding bacterial infection, in severely sick patients, antibiotics are generally given.
- If no infiltrates develop after 48 to 72 hours, antibiotics can be discontinued.

ASPIRATION PNEUMONIA

- The main stay of treatment is antibiotics.

Table 8.44: Empiric antibiotic therapy for aspiration pneumonia

Onset and Etiology	Characteristics	first-line	Second line
Community onset aspiration pneumonia	Mild to moderate (Able to tolerate oral)	Amoxicillin clavulanate 875 -1000mg mg, PO, BID x 7 days	Metronidazole (500 mg PO TID) + Amoxicillin (500 mg PO TID) For penicillin allergic patients: Clindamycin 450-600mg TID X 7days
	Severe (Need hospitalization and parenteral therapy)	Ampicillin-sulbactam (1.5 to 3 g IV QID) x 7 days	Ceftriaxone (1 or 2 g IV daily) + Metronidazole 500mg IV TID X 7days For patients with severe penicillin allergy: Clindamycin 600mg IV TID

Hospital onset aspiration pneumonia		Piperacillin-tazobactam 4.5g, Q 6hour x 7 days OR Meropenem 1gm IV Q 8hr OR Imipenem 500mg IV Q 6hr	Cefepime 2g IV Q8hr + Metronidazole 500mg IV TID
	If risk factor for MRSA, add vancomycin; if MRSA is not detected in a culture, discontinue it.		

PREVENTION

- The following preventive measures are important especially for at risk individuals (e.g., elderly, stroke etc.)
    - Avoiding intubation, when possible (noninvasive ventilation),
    - Minimizing transport of ventilated patients if feasible
    - Positioning (elevating head of bed, 30-to-45-degree angle)
    - Avoiding excessive sedation (e.g., avoiding sedative drugs in high-risk patients)
    - Maintain good oral hygiene, and treatment of dental and periodontal ailments can reduce bacterial colonization

FURTHER READING

1. L.A. Mandelland M. S. Niederman. Aspiration Pneumonia. N Engl J Med 2019;380: 651-63.
2. D. M. DiBardino and R. G. Wunderink. Aspiration pneumonia: A review of modern trends. Journal of Critical Care 30 (2015) 40-48

8.10.4.2 LUNG ABSCESS

BRIEF DESCRIPTION

- Lung abscess refers to a localized area of destruction of lung parenchyma, which results in tissue necrosis and suppuration.
- Most cases of lung abscess are complications of aspiration pneumonia caused by anaerobic microorganisms from the oral cavity (mainly gingival crevicesc).
- The typical patient with lung abscess risk factors to aspiration (e.g., alcoholism, general anesthesia, head trauma, dysphagia.)
- Lung abscesses are usually polymicrobial. The most common etiologies are anaerobic bacteria from the oral cavity: Peptosterptocooci, *Fusobacterium nucleatum, and Prevotella melaninogenica.*
- Pathogens that commonly produce pneumonia, such as *Streptococcus pneumoniae, Haemophilus influenzae, gram- negative bacilli (especially Klebsiella pneumoniae), and Staphylococcus aureus* may cause lung abscess.

CLASSIFICATION OF LUNG ABSCESS

- Acute versus chronic
  - Acute: present for less than one month
  - Chronic: Present for one or more month
- Primary versus secondary Primary:
  - Primary: resulting from aspiration of oropharyngeal secretions
  - Secondary: results from bronchial obstructions (by tumor, foreign body or enlarged lymph nodes) or with coexisting lung diseases (bronchiectasis, emphysema, lung contusion

CLINICAL FEATURES

- Indolent cough, fever, sputum production with night sweats
- Characteristically chills or rigors are absent

- Putrid (foul smelling) or sour-testing sputum: which most patients are aware
- Presence of gingival disease on examination
- Risk factors for aspiration

INVESTIGATION AND DIAGNOSIS

- Diagnosis of lung abscess should be considered in a patient who present indolent symptoms, risk factors for aspiration, and chest imaging (Chest X-ray or chest CT findings)
- Chest imaging: necessary for diagnosis
    - Chest X-ray: air-fluid level. Distinguishing between lung abscess and empyema with an associated air-fluid level can be challenging
    - Chest CT: If the lesion can't be delineated on the chest X-ray or if an associated mass lesion is suspected.
- Sputum: AFB stain, gram stain, aerobic culture

TREATMENT OBJECTIVES

- Achieve resolution of the abscess
- Treatment of the underlying cause: if treatable

NON-PHARMACOLOGIC

- Chest physiotherapy and position dependent drainage
- Surgery (Lobectomy or Pneumonectomy): Indications
    - Failure to respond to medical therapy after 12 weeks: after excluding other possible causes
    - Suspected malignancy or hemorrhage
    - Large ab scess > 6 cm

PHARMACOLOGIC

- The main stay of therapy for lung abscess is antibiotics.

EMPIRIC ANTIBIOTIC THERAPY FOR LUNG ABSCESS

- Anaerobic coverage is imperative (both strict and facultative anaerobes)
- Initial intravenous treatment

First line

- **Ampicillin-sulbactam** (1.5 to 3 g IV QID)

Alternatives:

- **Piperacilin/tazobactam** 4.5 grIV on 6 hr
- **Meropenem** 1 g IV on 8 hr
- **Penicillin G** 1 to 2 million units IV QID + Metronidazole 500 mg IV TID
- **Ceftriaxone** (1 or 2 g IV TID) + Metronidazole
- If there is severe penicillin allergy only: Clindamycin 600mg IV TID
- **Changing to oral therapy:** IV antibiotics need to be continued for a minimum of 2-3 weeks and marked resolution of symptoms occur.
    - Preferred oral agent: Amoxicillin-clavulanate 625mg TID OR 875-1000mg BID
    - For penicillin allergic: Clindamycin450-600mg PO TID
- Duration of therapy
    - There is no generally agreed-on duration.
    - 3-8 weeks of therapy is commonly used but it may need to be extended for few months.
    - If there is clinical improvement: do weekly or biweekly chest radiographs, discontinue therapy if there is small, stable lesion only on images.

FURTHER READING

1. Kuhajda I, Zarogoulidis K, Tsirgogianni K, et al. Lung abscess-etiology, diagnostic and treatment options. Ann Transl Med 2015;3(13):183.
2. Sabbula BR, Rammohan G, Akella J.Lung Abscess. Stat Pearls [Internet] 2020.

8.11 MENINGITIS (ACUTE BACTERIAL MENINGITIS)

BRIEF DESCRIPTION

- Meningitis is an inflammation of the meninges in response to an infection. It is mainly caused by bacterial infections (*S. pneumoniae, N. meningitides, and H. influenza*).
- Meningitis can also be causes by virus, (*Herpes simplex virus, Varicella zoster Enteroviruses, Cytomegalovirus, HIV, etc*), fungal infections (*Cryptococcus neoformans in immune-suppressed host*) or mycobacterium tuberculosis.
- There had been multiple epidemic meningitis (*N. meningitides* associated) in Ethiopia, occurring cyclically in 8-12 years, in strikingly seasonal pattern between January and May (dry and windy season).
- Acute meningitis is a reportable disease in Ethiopia.
- The disease is characterized by an intense headache, fever, vomiting, and photophobia with nuchal pain or rigidity and positive meningeal signs.
- Acute bacterial meningitis is a medical emergency associated with a very high mortality. Empiric antimicrobial therapy should be started promptly and LP should be done.

CLINICAL FEATURES

Symptoms

- The classic triad: fever, neck stiffness, change in mental status (defined as GCS <14)
- Headache

- Photophobia
- Seizures
- Al least two out of the four (fever, headache, stiff neck, change in mental status) is present in 95% of adults with bacterial meningitis.
- Presentation may be atypical (e.g., lethargy without fever) in the elderly and immunosuppressed. Hence, a very high index of suspicion in needed.
- A history of head trauma with or without skull fracture, the presence of a chronically draining ear and sinusitis is important.

Signs

- Nuchal rigidity
- Kernig's sign (patient supine, hip flexed at 90, knee flexed at 90): +ve if passive extension of knee results in involuntary resistance. Sensitivity is very low (~5%)
- Brudzinski's sign (patient supine): +ve if passive neck flexion if followed by involuntary hip and/or knee flexion). Sensitivity is very low (~5%)
- Funduscopic findings: papilledema, absent venous pulsations
- Focal neurologic findings: Cranial nerve palsies and occasional focal neurologic findings
- Skin rash: maculopapular, petechial, or purpuric (mainly meningococcal meningitis)

INVESTIGATIONS AND DIAGNOSIS

- Due to the very high mortality associated with it, a high index of suspicion is needed.
- The diagnosis of acute bacterial meningitis requires the following two findings:
  1. Consistent clinical presentation
  2. Diagnostic or suggestive CSF findings.

DIAGNOSTIC STUDIES

- Perform lumbar puncture (LP) prior to antibiotic administration: CSF analysis (cell count with differential, protein, glucose, gram stain, culture and sensitivity, Indian ink)
  - Gram stain: 60–90% sensitivity
  - Culture: 70–85% sensitivity
  - Other CSF findings: Markedly increased WBC (usually in thousands, with predominant neutrophils, very low glucose, increased protein)
- If LP is delayed or contraindicated (e.g., significant bleeding tendencies): take blood culture (2 bottles, if aviable) and start antibiotics without delay.

Table 8.45: Typical CSF findings in different causes of meningitis

Condition	Appearance	WBC/ mm^3 Predominant	Glucose (mg/dl)	Protein (g/l)	Remark
Bacterial	Cloudy, turbid	>100 to 10,000 (usually>1000) Polymorphs	<40 Very low	>1 (1-10)	Listeria meningitis may mimic viral
Tb	Clear Or Cloudy	>10 to few hundreds (usually 100-500) Lymphocytes	<40 Very low	>1	Early: the cells could be predominately neutrophils.

Fungal	Clear Or Cloudy	>10 to few hundreds (,1000) Lymphocytes	<45	<1	
Aseptic	Clear	>10 to few hundreds Lymphocytes	50-100	<1	

- Head CT to rule out mass effect before LP if presence of high-risk feature
  - ○ Age >60 years
  - ○ Immunocompromised
  - ○ Focal neurologic findings
  - ○ Papilledema
  - ○ History of CNS disease
  - ○ New-onset seizure or change in mental state

Algorithm: Management algorithm for adults with suspected bacterial meningitis

TREATMENT

- Acute bacterial meningitis is a medical emergency and the main stay of treatment is appropriate, high dose, intravenous antibiotics; hence, treatment should be started promptly.

OBJECTIVES

- Rapid eradication of the organisms from the CSF
- Prevent death and complications
- Amelioration of signs and symptoms

NON PHARMACOLOGIC

- Close supervision with regular monitoring of vital signs and neurological state.
- Institution of coma care for complicated cases.

EMPIRIC ANTIBIOTIC TREATMENT

- The choice of an empiric antibiotic for acute bacterial meningitis depends on the following factors
    - Age of the patient
    - Immunocompromised or not
    - Neurosurgery, penetrating head trauma or basal skull fracture
- Duration of therapy is 10 to 14 days. However, it can be adjusted if the specific causative pathogen is identified
    - Meningococcus: 7 days
    - Pneumococcus; 10- 14 days
    - *H. influenzae*: 7- 10 days
    - *Listeria monocytogenes*: at least 21 days
    - Gram negative bacilli: at least 21 days
    - *Staphylococcus aureus:* at least 14 days

Table 8.45: Empiric antibiotic recommendations for acute bacterial meningitis

Empiric therapy for COMMUNITY ACQUIRED acute bacterial meningitis		
Population	**First line**	**If anaphylaxis for B-lactams**
• 1 month - 50 years	Ceftriaxone + Vancomycin for 10-14 days	Vancomycin + Moxifloxacin
• >50 years	Ceftriaxone + Vancomycin + Ampicillin 21 days	Vancomycin + Moxifloxacin + Cotrimoxazole
• Immunocompromised • Alcoholism	Vancomycin + Ampicillin + Either of the following ○ Cefepime ○ Meropenem ○ Ceftazidime	Vancomycin + Meropenem + Cotrimoxazole
• Hospital acquired • Post- neurosurgery • Penetrating head trauma	Vancomycin + Either of the following ○ Cefepime ○ Meropenem ○ Ceftazidime	
• Basal skull fracture	Ceftriaxone + Vancomycin	

Table 8.46: Adult doses of antibiotics for the treatment of bacterial meningitis

Antimicrobial agent (AWaRe classification)	**Adult dose**
Ceftriaxone (Wa)	2 g IV 12 hourly
Cefotaxime (Wa)	2 g IV 6 hourly
Ampicillin (A)	2g IV q4h
Vancomycin (Wa)	1g IV BID
Ceftazidime (Wa)	2g IV q6-8h
Cefepime	2 g IV 8-12 hourly
Meropenem (Re)	2g IV Q8hr
Benzyl penicillin *(penicillin G)* (A)	20-24 million IU/dayIV in 4-6 divided doses
Chloramphenicol (A)	500mg I.V. QID
Cotrimoxazole (A)	20mg/kg per day divided Q6-12

A: access, Wa: watch and Re: reserve group antibiotic classification, WHO Aware database (https://aware.essentialmeds.org/groups)

SUPPORTIVE THERAPY

- Hydration: both under and over hydration may have unfavorable consequences.
- IV maintenance fluid IS preferred over restricted fluid intake in the first 48 hours in settings with high mortality and lately presenting patients.
- Nutrition support if required (NG tube feeding, if necessary)
- Analgesia and/or antipyretic:
  - Tepid sponging
  - Paracetamol oral, 1 g 4–6 hourly when required, maximum daily dose of: 4 g in 24 hours. Alternative: Ibuprofen, Diclofenac.

PREVENTION

- Prophylaxis of contacts: Close household contacts for H. influenza and N. meningitides. E. g. Ciprofloxacin, oral, 500 mg as a single dose.
- Avoiding sharing utensils or close contacts with people with upper respiratory tract infections.
- Prompt treatment of primary infection (e.g., upper respiratory tract infections)
- Using tissue or sleeve to cover sneezes and coughs and avoid kissing during infection.
- Avoiding overcrowding
- Proper hand washing and other peculiar precautions.
- Immunization as per national schedules (Ethiopia introduced H. influenza B vaccine (Hib) since 2007 and Pneumococcal Conjugate Vaccine (PCV) since 2013)
- Mass immunization if N. Meningitis epidemic (Men A vaccine is available in Ethiopia)

FURTHER READING

1. D. van de Beek, C. Cabellos, O. Dzupova et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clinical Microbiology and Infection, Volume 22 Number S37-S62, May 2016.
2. M J Griffiths, F McGill and T Solomon. Management of acute meningitis. Clinical Medicine 2018 Vol 18, No 2: 164-9
3. N Young and M Thomas Meningitis in adults: diagnosis and management. Internal Medicine Journal 48 (2018) 1294–1307

8.12 INFECTIOUS DIARRHEAL DISEASE

BRIEF DESCRIPTION

- Infectious diarrhea can occur as sporadic disease, in outbreaks or epidemics.

- Diarrhea could be acute (< 2wks) or chronic (>2 wks), watery or bloody.
- The commonest infectious causes of watery diarrhea: Viral diseases
- The commonest causes of bloody diarrhea: Bacterial.
- Other important etiologies: giardiasis (watery), amoebiasis (bloody/mucoid), and Schistosomiasis (predominately bloody)
- Clinical characterization of diarrhea in to acute/chronic, watery/bloody, and immunocompetent/immunocompromised host is important.
- In watery diarrhea: fluid and electrolyte replacement are the most important management. Antimicrobials have limited role.
- In bloody diarrhea: identification of pathogen and antimicrobial therapy is needed.

PREVENTION

- Preventive public health measures are important for the control of most acute diarrheal enteric infections.
- The following are key methods of preventing spread or microorganisms from person to person:
    - Hand washing with soap
    - Ensuring the availability of safe drinking water
    - Appropriate disposal of human waste
    - Safe handling and processing of food
    - Quality control of commercial products
    - Control of flies (particularly for Sd1)
    - Vaccination (e.g., monovalent and divalent cholera vaccines)

8.12.1 BLOODY DIARRHEA

8.12.1.1 BACILLARY DYSENTERY

BRIEF DESCRIPTION

- Bacillary dysentery is a diarrheal disease commonly caused by bacteria which invade and destroy the intestinal epithelium.
- Salmonella, Shigella, Campylobacter, E. coli are the dominant bacterial etiologies of bloody diarrhea.
- Transmission occurs via contaminated water or food
- Other non-bacterial causes of bloody diarrhea are Entameba histolytica and Schistosoma *mansoni.*

CLINICAL FEATURES

- Abdominal cramps, fever, and mucoid or bloody diarrhea with tenesmus.

INVESTIGATIONS AND DIAGNOSIS

- Direct stool examination which mostly reveals abundance of leukocytes (pus cells)
- Stool culture, if available, can be used to guide treatment selection

TREATMENT

OBJECTIVE

- Replace lost fluid and electrolyte
- Eradicate the infecting organism

SUPPORTIVE TREATMENT

- Correct dehydration with ORS (mild to moderate dehydration) or IV fluids (severe dehydration)
- Relieve pain and fever if necessary
- Anti-motility agents like loperamide should be avoided in patients with dysentery.

PHARMACOLOGIC

- Empiric treatment
    - **Ciprofloxacin** 500mg PO BID for 3-5 days are empiric first choice agents.
- Empiric treatment for Severe cases (septicemia):
    - **Ceftriaxone** 2g IV/day for 7-10 days
- Pregnant women: IV ceftriaxone 2gm IV/day for 3-5 days (mild to moderate) or 7-10 disease

FURTHER READING

1. M. S. Riddle, H. L. DuPont, and B. A. Connor. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. *Am J Gastroenterol*, 12 April 2016; doi: 10.1038/ajg.2016.126
2. Herbert L. DuPont. Acute Infectious Diarrhea in Immunocompetent Adults. N Engl J Med 2014; 370:1532-40.

8.12.1.2 AMEBIASIS (INTESTINAL)

BRIEF DESCRIPTION

- Intestinal amebiasis is caused by the protozoa *Entamoeba histolytica.* Most infections are asymptomatic.
- Clinical manifestations include amebic dysentery and extraintestinal disease (a
- The two common species of intestinal Entamoeba with identical morphology are E. histolytica, E. dispar. E. dispar is generally considered nonpathogenic.
- Most symptomatic disease is caused by E. histolytica.
- It is most commonly contracted through ingestion of alive cysts found with contaminated water, food, or hands.
- It is endemic in Ethiopia.

CLINICAL FEATURES

- Gradual development of lower abdominal pain and mild diarrhea
- Dysentery with frequent passage of stools (e.g., >10 stools per day)
- Stools are mostly blood and mucoid
- Malaise and diffuse lower abdominal
- If cecum is involved, signs and symptoms will mimic those of appendicitis (right lower quadrant pain)
- Other presentations: amoebic liver abscess, and ameboma (tender abdominal mass)

INVESTIGATIONS AND DIAGNOSIS

- Stool examination: Fresh stools specimens must be examined for trophozoites E. hemolytica.
- The non-pathologic E. dispar and the pathologic E. histolytica have similar morphology. Trophozoites that have ingested red blood cells are diagnostic of E. histolytica.

Treatment

Objectives

- Eradicate the trophozoites and improve clinical status; subsequently eradicate cysts to prevent relapses.
- Pharmacologic
- Treatment of invasive colitis consists of a tissue agent (e.g metronidazole) followed by a luminal (e.g., parmomycin) agent to eliminate intraluminal cysts.
- **Treatment of colitis**
    - **Metronidazole**, 500-750mg PO, TID for 7-10 days. For children: 7.5mg/kg PO, TID for 7-10 days.

      OR

  - **Tinidazole**, 2g PO once per day for 3 consecutive days. For children: 50-60mg/kg daily for 3 days.

- **Eradication of cysts**
  - **Diloxanide Furoate**, Adult 500mg 3 times daily PO, for 10 days. Child over 25kg, 20mg/kg daily in 3 divided doses for 10 days.

    OR

  - **Paromomycin**, 25–35mg/kg/day PO, divided in 3 daily doses for 7 days

FURTHER READING

1. J C. Carrero, M Reyes-López, J Serrano-Lunab et al. Intestinal amoebiasis: 160 years of its first detection and still remains as a health problem in developing countries. *International Journal of Medical Microbiology 310 (2020) 151358.*
2. Skappak, S Akierman, S Belga, et al. Invasive amoebiasis: A review of *Entamoeba* infections highlighted with case reports.Can J Gastroenterol Hepatol 2014;28(7):355-359.

8.12.2 WATERY DIARRHEA

BRIEF DESCRIPTION

- Watery diarrhea is usually the primary manifestation of an inflammatory or non-inflammatory response to intestinal tract infection.
- Viral diseases are the commonest causes of acute watery diarrhea. Rotavirus, Norovirus, and adenovirus are the commonly reported viral causes.
- Among the bacterial etiologies V*ibrio cholera and Escherichia coli* are important causes of watery diarrhea. Salmonella and listeria may need to be causes in high-risk patients.
- Giardia lamblia is an important protozoal etiology.
- Management considerations

- In the absence of fever, non-bloody, watery diarrhea is mainly due to viral infections.
- The main stay of treatment is rehydration and follow up for resolution of symptoms.
- Antimotility drugs e.g., Loperamide 4mg initially, then 2mg after every lose stool, maximum of 16mg/day
- Empiric antimicrobial therapy is not recommended for immunocompetent patients.
- If patients present with fever and significant abdominal pain investigation is needed (stool microscopy, stool culture and CBC)
- If watery diarrhea persists for more than a week, further investigation is needed.
- Watery diarrhea in people living with HIV should be approached differently: Salmonellosis, Girdiasis, Strongyloidosis, Cryptosporidium species, Cyclospora cayetanensis, should be considered.

8.12.2.1 CHOLERA

BRIEF DESCRIPTION

- Cholera is an acute diarrheal disease that can cause severe dehydration and death in a few hours. I
- It is caused by Vibrio cholera and often occurs as epidemics under conditions of poor hygiene.

CLINICAL FEATURES

- Sudden onset of explosive diarrhea is the hallmark of the disease.
- The diarrhea is classically voluminous, non-offensive, and somewhat looks gray or "rice water".
- Fever is absent.

INVESTIGATIONS AND DIAGNOSIS

- It is often diagnosed based on clinical grounds.
- If possible, stool culture.

Treatment

Objectives

- Correction of fluid and electrolyte deficits
- Replacement of ongoing fluid losses
- Decrease duration of diarrhea

PREVENTION

- The promotion of adequate hygienic conditions in the community is important to prevent an outbreak and spread of the disease.
- If cholera outbreak is suspected, the responsible heath authorities should be notified.Appropriate epidemic investigation and confirmation is needed.
- Patients should be treated in isolated area with infection prevention strategies in place, trained manpower and "cholera-beds'
- Individual case management
    - The main stay of treatment is rehydration.
    - Assess the level of dehydration (volume status): through simple examination of the mental status, eyes, mouth, skin, pulse and BP.
    - The degree of volume depletion can be categorized by WHO criteria of no, some or severe dehydration.
    - For adults' mild dehydration and no significant vomiting: ORS (oral rehydration solution) should be given to be taken as tolerated per each bowel motion.
    - For adults with severe dehydration or hypovolemic shock
        - Secure IV line with a wide bore needle, preferably two IV lines.

- Ringer's lactate IV is the preferred fluid (Use normal saline, if only Ringer's lactate is not available)
- **Volume**:
    - 100ml/kg for the first three hours (7 liters for a 70kg adult)
    - The first 30ml/Kg (2 liters) should be given fast (30 minutes)
    - The remaining 70ml/kg (5 liters) in the remaining 2 1/2 hours.
    - Adults with severe cholera require about 200ml/Kg or more (14 liters or more) in the first 24 hours
    - Ongoing loss should be assessed and further replacement should be assessed based on ongoing losses.
    - Oral fluid intake (ORS should be started) as soon the patient condition improves and is able to take orally.
- Potassium
    - KCl solution 20 -40 mmol/liter needs to be added after the initial 3 hours resuscitation.
    - If serum potassium can be determined, it should be followed closely.

- Antibiotics

First line

- **Doxycycline** 300mg PO stat

Alternatives

- **Tetr**acycline 500mg QID for 3 days.
- **Sulfamethoxazole+trimethoprim**: 800mg/160mg PO BID for 3 days.
- **Ciprofloxacin,** 1000mg PO stat or 500mg P.O., BID, for 3 days

PREVENTION

- Clean water supply: Water treatment with chlorination or boiling when there is no clear water supply
- Sanitation and hygiene

FURTHER READING

1. Guideline on CHOLERA OUTBREAK MANAGEMENT Ethiopia. Ethiopian Health and Nutrition Research Institute May 2011.
2. Management of the patient with cholera. WHO/CDD/SER/91.15 REV.1

8.12.2.2 GIARDIASIS

BRIEF DESCRIPTION

- *Giardia lamblia* is a ubiquitous gastrointestinal protozoon.
- It may result in clinical presentation that ranges from asymptomatic colonization to acute or chronic diarrheal illness.
- It can occur both sporadically and in epidemics.
- *Giardia lamblia* infects humans through ingestion of as few as 10 cysts.
- The infection is more prevalent in children than adults. Asymptomatic infection occurs in approximately 60% of people exposed to Giardia.

CLINICAL FEATURES

- Clinical features vary from asymptomatic, acute, and chronic giardiasis
- Asymptomatic infection: no symptoms but cyst shedding
- **Acute giardiasis**:
  - Watery diarrhea
  - Foul-smelling and fatty stools (steatorrhea), malabsoprption
  - Abdominal cramps and bloating

  - Malaise
  - Flatulence
  - Nausea and/or vomiting
  - Weight loss
- **Chronic giardiasis**
  - Loose stools but usually not diarrhea
  - Steatorrhea, profound weight loss (10 to 20%), malabsorption
  - Malaise, Fatigue
  - Abdominal cramping
  - Borborygmi, Flatulence, Burping

INVESTIGATIONS AND DIAGNOSIS

- Stool microscopy: identifying Giardia lamblia trophozoite or cyst from
- Limitation of stool microscopy: due to intermittent shading of cysts stool microscopy can be negative; hence, it should be repeated about three times, if the initial one or two are negative. It also needs technician expertise.

TREATMENT

OBJECTIVES

- Correct fluid and electrolyte abnormalities
- Improve symptoms
- Eradicate the protozoa

SUPPORTIVE TREATMENT

- Assess hydration status, electrolytes and nutritional status: correction of fluid and electrolyte deficits.

ANTIMICROBIAL THERAPY

First line

- **Tinidazole:** 2g PO single dose, for adults. For children > 3 years of age, 50 mg/kg orally, single dose (maximum dose 2 g).

Alternatives

- **Metronidazole**: 500mg BID or 250mg TID X 5-7 days for adults. For children 15mg/kg in three divided doses (maximum 250mg per dose).
- **Albendazole**: 400 mg orally once daily x 5 days for adults. For children 10 to 15 mg/kg orally once daily X 5 days (maximum 400 mg per dose).
- **Mebendazole**: 200mg PO TID X 5 days, for both adults and children.
- First trimester pregnancy:
  - Delay treatment if symptoms are mild
  - If symptoms are significant and treatment is mandatory: Paromomycin 10 mg/kg orally three times per day for 5 to 10.
- Second and trimester pregnancy: Tinidazole or metronidazole.

Prevention: Infection prevention and control measures are important including:

- Avoid drinking water or eating foods which is potentially contaminated (E.g., purify drinking water, do not swallow water while swimming, and eat cooked foods at least in risk conditions).
- Strict hand washing with water and soap, alcohol-based hand rubs cysts
- Carful diaper disposal and treatment of symptomatic children will prevent spread.
- Breastfeeding is protective against giardiasis in nursing infants in endemic areas
- Zinc and vitamin A supplementation is associated with a protective effect in children

FURTHER READING

1. C. Minetti, R M Chalmers, N J Beeching et al. *BMJ* 2016;355: i5369

2. T B. Gardner and D R. Hill.Treatment of Giardiasis Clinical Microbiology Reviews. Jan. 2001, P. 114–128 Vol. 14, No. 1

8.12.2.3 CLOSTRIDIOIDES DIFFICILLE ASSOCIATED DISEASE (CDAD)

Brief description

- *Clostridioides (formerly Clostridium) difficile* associated disease (CDAD) results from a disturbance of the normal bacterial flora of the colon, colonization by *C difficile*, and the release of toxins.
- The strongest risk factor for CDAD is recent antibiotic use.
- In addition to recent antibiotic use the following are important risk factors:
  - Elderly
  - ICU admission
  - Kidney failure
  - Burn patients
  - Abdominal surgery
  - Chemotherapy
  - Immune-compromised
- All classes of antibiotics are potentially associated with CDAD.The highest CDAD risk is associated with clindamycin, fluoroquinolones, and broad spectrum cephalosporins and penicillins.
- Symptoms may occur from the time while the patient are still receiving antibiotic to 2 to 10 weeks after completion of antibiotics.The commonest time is after 5- 10 days of therapy.
- Recurrence is common.

CLINICAL FEATURES

- **Non-**severe disease

  - Watery diarrhea (≥3 loose stools in 24 hours) is the cardinal symptom.
  - Diarrhea may have mucus and occult blood.
  - Nausea, lower abdominal pain and cramping
  - Low-grade fever
  - Lower abdominal tenderness.
  - Unexplained leukocytosis (<15,000) in hospitalized patients
- **Severe and fulminant colitis**
  - Diarrhea, lower quadrant or diffuse abdominal pain,
  - Abdominal distention
  - Fever, hypovolemia
  - Marked leukocytosis (> 15,000, up to 40,000 or higher)
  - Elevated creatinine (>1.5mg/dl)
- **Fulminant colitis**: hypotension or shock, ileus, or megacolon

Table 8.47: Severity classification of CDAD

Severity classification	Parameters
1. Non-severe	WBC <15,000/ml **and** a serum creatinine <1.5 mg/dl
2. Severe	WBC >15,000/ml **or** a serum creatinine >1.5mg/dl
3. Fulminant	Hypotension/shock **or** ileus **or** megacolon

INVESTIGATIONS AND DIAGNOSIS

- Diagnosis requires a high index of suspicion is needed: patients with risk factors who have unexplained diarrhea (>3 loose stools/day) with leukocytosis should be evaluated for CDAD.
- Diagnosis requires liquid stool samples test for toxin with either glutamate dehydrogenase (GDH) or nucleic acid amplification test (NAAT).

- Stool exam: shows pus cells and may be heme positive.
- CBC, serum creatinine and electrolytes.
- Colonoscopy: pseudomembranous colitis

N.B. As the tests for the diagnosis of CDAD are not commonly available in Ethiopia, in patients suspected to have severe or fulminant disease empiric treatment should be started without any delay

Treatment

Objectives

- Correct fluid and electrolyte deficit
- Arrest diarrhea and to prevent recurrence of diarrhea.

Non-Pharmacologic

- Discontinue offending agent is the initial step.
- Infection control, including contact precautions and hand hygiene.

Pharmacologic

- Oral vancomycin is the first line of therapy. As vancomycin oral capsule is not available, the powder for intravenous use can be prepared for oral administration as follows
  - ○ Reconstitute one 500mg vancomycin vial powder with 10ml or a 1000mg vial with 20ml of water for injection.
  - ○ Withdraw 2.5ml (125mg) and mix again with 30ml of water.
  - ○ For flavoring juice can be added immediately before giving.
  - ○ Document the time and date on the remaining vial.
  - ○ Store the reconstituted vial in fridge. It can only be used for 24 hours.

Table 8.48: Empiric antibiotic treatment recommendations for C.difficile in adults

	First line	**Second line**
Non-severe	Vancomycin 125 mg PO QID for 10 days	Metronidazole 500 mg PO TID for 10 days
Sever	Vancomycin 125 mg PO QID for 10 days,	
Fulminant colitis	Vancomycin 500 mg orally or via NG tube QID PLUS Metronidazole 500 mg IV TID	
Recurrent CDI	Vancomycin pulsed-tapered regimen: 125 mg PO QID for 10-14 days, then 125 mg PO BID for 7 days, then 125 mg PO daily for 7 days, then 125 mg PO every 2/3 days for 2 to 8 weeks	

- In patients who are unable to take oral medications, intravenous metronidazole can be used. Intravenous vancomycin fails to achieve significant intraluminal bowel concentrations and is not recommended.
- Avoid other antiperistaltic agents as they may cause toxic megacolon.
- Fecal transplant (GI colonization by nontoxigenic C. difficile strains) in recurrent relapse

PREVENTION

- Restricting antibiotic use particularly during the outbreaks (e.g., Clindamycin restriction)

- Keep patients with suspected CDAD in a single room with separate toilet, if available.
- Contact precautious should be in place
- Hand hygiene with soap and water. Alchol hand rubs are not as effective as soap and water in removing *C. difficile* spores.

FURTHER READING

1. L. C McDonald, D N. Gerding, S Johnson et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clinical Infectious Diseases 2018:66 (1 April)
2. M Sartelli1, S Di Bella, L V. McFarland et al. 2019 update of the WSES guidelines for management of Clostridioides (Clostridium) difficile infection in surgical patients. World Journal of Emergency Surgery (2019) 14:8https://doi.org/10.1186/s13017-019-0228-3

8.13 PYOGENIC OSTEOMYELITIS

BRIEF DESCRIPTION

- Pyogenic Osteomyelitis is an acute infection of the bone and its structures caused by bacteria.
- Osteomyelitis occurs as a result of hematogenous spread, contiguous spread from adjacent soft tissues or direct infection from trauma or surgery.
- Hematogenous osteomyelitis is usually monomicrobial, while osteomyelitis due to contiguous spread or direct inoculation is usually polymicrobial.
- Staphylococcus aureus is the most common causative organism. Coagulase- negative staphylococci and aerobic gram-negative bacilli are also common causes. Streptococci, enterococci and anaerobes are also implicated.

- Osteomyelitis can be acute or chronic
- Anatomically and physiologically osteomyelitis is classified by

Table 8.49: Cierny-Mader's osteomyelitis classification system

Anatomical type	Physiological condition	Remarks
Type I: Medullary	A: Healthy	**Systemic factors** (Bs): Malnutrition, CKD, liver failure, DM, chronic hypoxia, neonate/elderly, malignancy, immunosuppression Local factors (Bl): Chronic lymphedema, venous stasis, major vessel compromise, arteritis, large scar formation, post-radiation fibrosis, small-vessel disease, neuropathy or smoking
Type II: Superficial	B: Systemically compromised, Bs	
Type III: Localized	Locally compromised, Bl	
Type IV: Diffused	Systemically and locally compromised, Bls	
	C: The majority of damage is due to treatment rather than disease	

CLINICAL FEATURES

- **Acute osteomyelitis**
  - Gradual onset of symptoms over several days.
  - Dull pain at the involved site
  - Fever may be present
  - Local findings: tenderness, warmth, redness, and swelling
  - Acute osteomyelitis can also locally spread to the joint, presenting as septic arthritis
  - Patients with hip, vertebrae, or pelvis osteomyelitis may have few signs or symptoms

- **Chronic osteomyelitis**
  - May present with pain, swelling with or without erythema
  - A draining sinus tract: almost pathognomonic
  - Ulcer which fails to heal after several weeks should raise suspicion for chronic osteomyelitis

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis osteomyelitis requires imaging evidence
- When osteomyelitis is suspected clinically: X-ray of the involved area should be done.
- If plain radiographs are normal: other imaging modalities need to be done; MRI is preferred over CT scan.
- Other lab tests: ESR/CRP, CBC
- Blood cultures
- Culture from debrided bone tissue or biopsy

TREATMENT

OBJECTIVES

- Control infection and sepsis
- Prevent disability

Non pharmacologic

- Rest/immobilization
- Surgical debridement in acute osteomyelitis: indications
  - Radiologic evidence of necrosis or abscess
  - Failure of antimicrobial therapy alone
- Surgery in chronic osteomyelitis: most patients need surgical/orthopedic evaluation for debridement of necrotic tissue, management of dead space, stabilization of bony structures and reconstruction of soft tissue.

PHARMACOLOGIC

Empiric antibiotic treatment

- Empiric treatment with activity against Staphylococcus aureus (especially MRSA) and gram-negative organisms is required.

First line

- **Vancomycin**, 30mg/kg/day, IV, in two divided doses (initially 20 mg/kg loading dose, not to exceed 2 g/dose)

PLUS

- **Ceftriaxone** 2 g IV every 24 hours **OR** Ciprofloxacin, 400 mg IV q12 hours or 750mg, PO BID

Alternative

- **Cloxacillin**, 2gm, I.V. QID

PLUS

- **Ciprofloxacin**, 400 mg IV q12 hours or 750mg, PO BID

Specific antimicrobials: once susceptibility results are available, specific drugs should be used.

Duration of antimicrobial therapy: At least 6 weeks from the last debridement.

Monitoring

- Clinical response
- ESR and CRP: If persistently elevated after two weeks, persistent osteomyelitis should be suspected.
- Weekly complete blood count weekly
- RFT and LFT every 1-2 weeks

REFERRAL

Patients with osteomyelitis should be treated in hospitals with orthopedic surgical service.

FURTHER READING

1. The Korean Society for Chemotherapy, et al • Clinical Guidelines for the Antimicrobial Treatment of Bone and Joint Infections in Korea. Infect Chemother 2014;46(2):125-138. http://dx.doi.org/10.3947/ic.2014.46.2.125
2. J Hatzenbuehler and T J. Pulling Diagnosis and Management of Osteomyelitis. Am Fam Physician. 2011;84(9):1027-1033.

8.14 SEPTIC ARTHRITIS

BRIEF DESCRIPTION

- Septic arthritis refers to bacterial infection and the resulting inflammatory destruction of joints.
- Septic arthritis is highly destructive to the joint and is considered a medical emergency.
- It is commonly hematogenous in origin (80-90%), contiguous spread (10-15%), and direct penetration of microorganisms secondary to trauma, surgery or injection.
- It is more common in children. In adults old age, diabetes mellitus, skin infection, alcoholism, intra-articular steroid injections are some of the common risk factors.
- Staphylococcus aureus is the most common cause. Group B Streptococci and other gram positive are also frequent causes. Gram-negative bacilli are found as causes in specific situations such as trauma, immunosuppression and very elderly.
- Gonococcal arthritis is an infectious arthritis which should be considered in sexually active young adults with culture negative arthritis.
- Septic arthritis is generally monoarticular or oligoarticular. Poly articular septic arthritis might occur in patients with rheumatoid arthritis or other connective tissue diseases.

- Knee is the commonest involved joint. Wrist, ankle, and hip joints are other commonly affected joints.

CLINICAL FEATURES

- Joint pain, swelling, warmth
- Restricted movement
- Fever: Chills and rigors are not usually present
- Evidence for the focus of infection: Skin, pulmonary, urinary tract infection

INVESTIGATIONS AND DIAGNOSIS

- Joint (synovial fluid) fluid aspiration
  - Fluid should be aspirated before initiation of antibiotics.
  - The diagnosis of septic arthritis needs synovial fluid analysis.
  - Definitive diagnosis requires identification bacteria in the synovial fluid: gram stain and/or culture.
  - Synovial fluid WBC count is usually >50,000/mm3 with predominate neutrophils but a cell count <50,000/mm3 does not exclude the diagnosis.
  - Synovial fluid glucose and protein are not useful in the diagnosis.
- Blood culture should be taken before starting antibiotics
- CBC, ESR/CRP
- X-ray of the affected joint: to evaluate for possible associated osteomyelitis
- Echocardiography: in patients with evidence of valvular heart disease to evaluate for possible infective endocarditis

TREATMENT

OBJECTIVES

- Prevent joint destruction and disability
- Prevent sepsis and its complication

JOINT FLUID DRAINAGE

- All patients with septic arthritis need joint fluid drainage. The options are the following
  - Needle aspiration (arthrocentesis): repeated aspirations until the effusion resolves
  - Arthroscopic drainage
  - Arthrotomy (open surgical drainage)
  - Indications for surgical drainage: hip joint involvement, failure to responds with needle aspiration and antibiotics after 5-7 days
- Splintage/immobilization may be needed for pain relief; however early mobilization is encouraged once there is improvement.

PHARMACOLOGIC (ANTIBIOTICS)

- As septic arthritis is destructive, empiric intravenous antibiotics should be started immediately after taking synovial fluid samples.

EMPIRIC ANTIBIOTICS

- The initial empiric antimicrobial choice should cover the most likely pathogens. If the facility cannot carry a gram stain analysis the following regimen is generally recommended.

First line

- **Vancomycin**, 30mg/kg/day IV in two divided doses, not to exceed 2g per day

PLUS

- **Ceftriaxone**, 2gm, IV, once daily or cefotaxime 2 g IV TID

Alternatives

- **Cloxacillin**, IV, 2g every 6 hr QID for 4-6 weeks

OR

- **Ceftriaxone** 2gm, IV, once daily or cefotaxime 2 g IV TID

ANTIBIOTICS BASED ON GRAM STAIN RESULTS

- Gram-positive cocci:

First line

- **Vancomycin** (as above)

Alternative

- **Cloxacillin (as above)**
- **Gram** negative bacilli:
  - **Ceftriaxone** or **cefotaxime** (as above)
- Gram-negative cocci or clinical syndrome suggestive of disseminated gonococcal infection
  - **Ceftriaxone** 1 g IV once daily PLUS Azithromycin 1 g orally (single dose)
  - Negative gram stain
    - **Vancomycin** alone in immunocompetent adults
    - **Vancomycin** PLUS Ceftriaxone

DURATION OF ANTIBIOTIC THERAPY

- A total of 4-6 weeks: At least the first two weeks should be IV followed by oral. Typically, 2 weeks IV and 2 weeks oral.

Referral

- Patients with septic arthritis should be managed in consultation of orthopedic surgeon of possible arthroscopic or open drainage. However, needle aspiration of the joint and empiric antibiotics should be started as soon as possible.

FURTHER READING

1. John J. Ross. Septic Arthritis of Native Joints. Infect Dis Clin N Am 31 (2017) 203–218.

2. C J Mathews, V C Weston, A Jones et al. Bacterial septic arthritis in adults. *Lancet* 2010; 375: 846–55
3. K A. Sharff, E P. Richards and J M. Townes. Clinical Management of Septic Arthritis. Curr Rheumatol Rep (2013) 15:332.

8.15 NEUTROPENIC FEVER

BRIEF DESCRIPTION

- An absolute neutrophil count (ANC) <1,500/µl is defined as neutropenia; if the ANC is <500/µl it is defined as severe neutropenia. ANC = (Total WBC X % of neutrophils) ÷ 100.

The term profound neutropenia is used when ANC is less than 100/µl.

- Fever is defined as a single oral temperature > 38.3^{0}c or an oral temperature >38^{0}c sustained for an hour or more. Axillary temperatures are on average 0.5^{0}c less than oral temperature records; hence, an axillary temperature >37.5^{0}c should be considered as febrile.
- Neutropenic fever is a documented fever in patients with ANC< <1,500/µl.
- There are several causes of neutropenia; the major ones are cancer chemotherapy, hematologic malignancies, autoimmune diseases, infectious diseases and congenital (inherited).
- Cancer chemotherapy associated neutropenia is a major concern due to a marked increase in mortality in patients with neutropenic fever.
- Both the duration and the severity of neutropenia increase the risk of infection and bad outcome. The more prolonged or profound the neutropenia is, the outcome is worse.
- The outcome of patients with cancer associated neutropenic fever depends on several factors. One of the most widely used risk scores is the MASCC score (See the table below)

Table 8.50: MASCC (Multinational Association for Supportive Care in cancer) febrile neutropenia risk index

Burden of illness: no or mild symptoms	5
Burden of illness: moderate symptoms	3
Burden of illness: severe symptoms	0
No hypotension (systolic BP > 90 mmHg)	5
No chronic obstructive pulmonary disease	4
Solid tumour/lymphoma with no previous fungal infection	4
No dehydration	3
Outpatient status (at onset of fever)	3
Age <60 years	2
Scores ≥21: low risk of complications **Scores< 21 high risk**	

- Neutropenic fever syndromes are divided in to three
    - **Microbiologically documented infection**: when there is a focus of infection and isolated microorganism
    - **Clinically documented infection**: when there is a focus (e.g., pneumonia, cellulitis, urinary tract infection) but no isolated organism
    - **Unexplained fever**: when there is no clear focus.
- Common causative pathogens
    - Gram negatives are the most common causes of neutropenic fever in both high risk and low risk patients: Enterobacteriaceae (e.g., *Escherichia coli*, *Klebsiella* sp), *Pseudomonas aeruginosa*, *Acinetobacter* sp, *Stenotrophomonas maltophilia*).
    - Gram-positive cocci (e.g., *Staphylococcus aureus*, coagulase-negative staphylococci, streptococci, enterococci)
    - Fungal infections are less common in low-risk patients but they are important causes in high-risk patients.

  - Reactivation of herpes simplex virus and varicella-zoster virus can also be causes.

CLINICAL FEATURES

- Fever: Regular and appropriate recording of fever. Do not use rectal temperature measurement
- Tachypnea, tachycardia, hypotension
- Focus of infection:
  - IV cannulas/ central lines
  - Urinary catheters
  - Symptoms or signs suggesting an infection focus: Respiratory, GI, skin, oropharynx, perineal region, genital discharge, CNS symptoms

INVESTIGATIONS

- Routine investigations: If there is clinically focus, do site specific investigations.
  - Blood cultures (minimum of two sets) including cultures from indwelling IV catheter
  - Urinalysis and culture
  - Stool microscopy and culture
  - Sputum microscopy and culture
  - Renal and liver function test
  - Skin lesion (aspirate for culture)
  - Chest X-ray
- Further investigations (profound/prolonged neutropenia)
  - High-resolution chest CT (if fever persists > 72 h of appropriate antibiotics)

TREATMENT

OBJECTIVES

- Prevent morbidity related to the infection/s.
- Improve cancer treatment outcome

EMPIRIC INITIAL THERAPY FOR HIGH-RISK PATIENTS

- Antibiotics should be started as quickly as possible after taking samples for culture.

MONOTHERAPY WITH AN ANTIPSEUDOMONAL AGENT

- **Carbapenems** (Meropenem or imipenem)

OR

- **Cefepime**

OR

- **Piperacillin tazobacatam**

ADDITION OF VANCOMYCIN IN THE INITIAL REGIMEN

- Vancomycin is not recommended as part of the initial regimen. However, it should be added in patients with any of the following findings
- Hemodynamic instability or other signs of severe sepsis
- Pneumonia
- Skin or soft tissue infection
- Severe mucositis
- Suspected central venous catheter (CVC)-related infection
- Positive blood cultures for gram-positive bacteria while awaiting speciation

Consideration for anaerobic coverage in the initial regimen: If one of the followings are found use carbapenems or piperacillin tazobactam in the initial regimen as they also cover anerobes. If Cefepime is used add metronidazole.

- Evidence of perianal infection, necrotizing gingivitis
- Potential intraabdominal infection or severe diarrhea

Addition of antifungal (Fluconazole) or antiviral (Acyclovir) in the initial regimen: in patients with esophagitis

Reassess response to treatment on day 3 (after 48 hour of therapy)

- Persistent fever alone in an otherwise stable patient is not sufficient justification for modification of the initial antibiotic regimen
- If fever is persisting and the patient is clinically worsening
- If the initial regimen was not a carbapenem, change the antibiotic to a carbapenem
- If the initial regimen was a carbapenem based regimen, consider adding aminoglycoside.
- If the initial regimen did not contain vancomycin add vancomycin

PERSISTENT FEVER AND NEUTROPENIA BY DAY 5

- Add an antifungal agent (e.g., Fluconazole, amphotericin B product or caspofungin)

LOWER-RISK PATIENTS

- Low risk patients can be managed as outpatients, following a short hospital admission.
- An eight-hour monitoring or one day admission after the initial dose of antibiotics might be good before sending them home.
- Patients that cannot access medical care within hours or those with fever recrudescence or new signs of infection should be managed in the hospital.
- Empiric regimens for low-risk patients:
    - **Ciprofloxacin** 750 mg PO BID PLUS **Amoxicillin–clavulanic** acid (500 mg/125 mg TID)

DURATION OF ANTIBIOTIC THERAPY

- Stop antibiotic therapy when neutrophil count is ≥500 cells/mm3 for 2 consecutive days and patient is afebrile for ≥48 hours if
    - No evidence of focal infection
    - Cultures are negative
- Continue antibiotic therapy for 4-5 days after neutrophil count is ≥500 cells/mm3 if fever persists.
- If patient remains febrile and neutropenic with no other evidence of infection, continue anti- infective agents for 2 weeks, followed by clinical reassessment and consideration of discontinuation of antibiotic therapy

OTHER CONSIDERATIONS

- In patients with severe penicillin allergy consider use of ciprofloxacin, or aminoglycoside for coverage of gram-negative organisms
- Guide choice of empiric antimicrobials by local or institutional antibiotic resistance profiles
- Consider removal of vascular catheter.

Table 8.51: Antimicrobial dosing for neutropenia fever management in adults with normal renal function

Drug	Dose	Comment
Ciprofloxacin	750 mg orally twice daily	First line for low risk with amoxicillin–clavulanic acid
Amoxicillin–clavulanic	500 mg/125 mg orally three times daily or 1000 mg/250 mg orally twice daily	First line for low risk with fluoroquinolones
Clindamycin	300 mg four times daily	Use in place of amoxicillin for low-risk patients
Cefixime	400 mg once daily	
Cefepime,	2 g IV every eight hours	First line for high risk or low risk with previous fluoroquinolone use

Piperacillin	4.5 g IV every six to eight hours, use QID if risk for resistant infection is high.	Second line in place of Cefepime
Ceftazidime,	2 g IV every eight hours	Second line in place of Cefepime
Meropenem	1 g IV every eight hours	Third line, used only if no other first line and second line agents (use imipenem if Meropenem is not available)
Imipenem and cilastatin,	500mg every 6 hours	
Vancomycin	1 g IV every 12 hours	add for those with MRSA risk

Prevention

- Hand hygiene and cough etiquette is the most important prevention method for the spread of respiratory virus infections in ambulatory low-risk cancer patients.
- G-CSF prophylaxis: to be decided based on the risk by specialists involved in the care.
- Antimicrobial prophylaxis is required for high-risk patients depending on the potential risk for different pathogens.

FURTHER READING

1. J. Klastersky, J. de Naurois, K. Rolston et al. Management of febrile neutropenia: ESMO Clinical Practice Guidelines. Annals of Oncology 27 (Supplement 5): v111–v118, 2016
2. PERSPECTIVES IN FEBRILE NEUTROPENIA: Guidelines in the Management of Febrile Neutropenia for Clinical Practice. AJMC: Evidence-Based Oncology OCTOBER 2017; 9-13

8.16 SEPSIS AND SEPTIC SHOCK

BRIEF DESCRIPTION

- **Sepsis** is now defined as life threatening organ dysfunction caused by dysregulated host response to infection.
- Sepsis is caused by the immune response triggered by an infection. The infection is most commonly bacterial. Fungi, viruses, or parasites can also cause sepsis.
- Organ dysfunctions that should lead to consideration of sepsis:
    - Respiratory: hypoxia
    - Cardiovascular: hypotension
    - Brain: depressed mental status
    - Renal: oliguria or rising creatinine
    - Liver: increased bilirubin
    - Low platelet
    - General hypoperfusion: elevated serum lactate
- Septic shock is defined in patients who have sepsis, despite adequate fluid resuscitation, require vasopressors to maintain a mean arterial pressure (MAP) ≥65 mmHg and have a lactate >2 mmol/L (>18 mg/dl).
- Sepsis and septic shock are the major causes of morbidity and mortality worldwide.
- The most common primary sources that lead to sepsis were respiratory tract, urinary tract, skin, CNS, and abdominal organ infections.
- Old age, immunocompromising such cancer, diabetes, HIV and major trauma or burns are major risk factors for sepsis.

CLINICAL FEATURES

- Fever, tachycardia, tachypnea, hypoxia (low oxygen saturation)

- Warm, flushed skin may be present in the early phases of sepsis
- Hypo perfusion signs: delayed capillary refill, low BP, decreased urine output
- As sepsis progresses to shock, the skin may become cold.
- Oliguria or anuria.
- Altered mental status, obtundation or restlessness
- Ileus or absent bowel sounds: an end-stage sign
- Symptoms related to a specific site of infection:
    - Cough, purulent sputum, shortness of breath: pneumonia
    - Dysuria, frequency, urgency, flank pain: urinary focus
    - Diarrhea (bloody), abdominal: GI focus
    - Lower abdominal pain, vaginal discharge: pelvic focus
    - Pustules, ulcers, localized painful erythematous skin lesion: skin focus
    - Headache, neck stiffness: CNS focus
- In the elderly and immunocompromised patients, symptoms of a specific infection may not present and the body temperature may be low or normal rather than high.

INVESTIGATION AND DIAGNOSIS

- Screening for sepsis
    - Due to the non-specific nature of the presentation but the increased mortality associated with sepsis, screening tools are utilized to identify patients early.
    - Systemic inflammatory response syndrome (SIRS) is no more recommended.
    - The **quick SOFA** (sequential Organ Failure Assessment) score (qSOFA) is a simple and practical bedside tool for screening adult patients for sepsis with high likelihood of poor outcome.

- ○ qSOFA: if an adult patient in a non-ICU setting meets at least 2 of the following 3 clinical criteria, the qSOFA is positive.
  - Respiratory rate > OR =22/minute
  - Altered mentation
  - Systolic blood pressure < OR = 100 mmHg
- ○ A positive a qSOFA score should prompt the following cations
  - A consideration of sepsis if it has not been considered
  - Initiation of investigation: organ dysfunction, cultures and imaging
  - Revision or initiation of antibiotic therapy
  - Frequent monitoring or consideration of transfer to ICU

INVESTIGATIONS

- CBC
- Serum lactate (serial measurements needed if available)
- Asses organ dysfunction: RFT and LFT
- Cultures
- Blood culture: At least two sets of blood cultures (aerobic and anaerobic) from different sites
- Culture form indwelling vascular catheters, urine, skin lesion depending
- Take prior to antibiotic administration as long as it does not cause a delay.
- Imaging of suspected sources: e.g. Chest X-ray or pneumonia

TREATMENT

OBJECTIVES

- Timely diagnosis and identification of pathogen
- Prevention of progression to shock, organ failure and decrease

mortality

TREATMENT APPROACHES IN SEPSIS

- Sepsis and septic shock are medical emergencies
- **Hour -1 bundle**: A set of measures to be taken in the first hours
  - Secure airway, administer oxygen to keep SPO2 > 94%
  - Obtain blood culture before starting antibiotics. However, it should not delay antibiotic initiation beyond one hour.
  - Administer broad-spectrum IV antibiotics
  - If hypotensive give IV fluids rapidly (crystalloids, preferably RL) 30ml/kg (the 30ml/kg should be completed in maximum of 3 hours)
  - If hypotension persists during or after fluid resuscitation start vasopressor without any delay to maintain mean arterial pressure $\geq$65mmHg.
- **Early measures**
  - IV fluids: Complete the 30ml/kg (about 2 liters) within three hours and it can be repeated if BP fails to respond.
  - Restrict IV fluid and closely monitor those with heart failure, kidney disease and cirrhosis
  - Monitor BP and hourly urine output.
  - Assess for signs of pulmonary edema (due to aggressive fluid resuscitation).
  - IV fluids may be unhelpful or harmful when the circulation is no longer fluid responsive.
- **Consecutive measures**
  - Vasopressor: if hypotension is refractory to the initial fluid resuscitation start vasopressor.
  - Norepinephrine (noradrenaline) is the preferred agent

  - Initial dose: 0.1 to 0.15 mcg/kg/minute (7 to 12mcg/minute).
  - Norepinephrine dilution: a usual concentration is 4 mg in 250 mL of D5W or NS = 16 micrograms/ml
  - Maintenance dose: 2 to 4 mcg/minute (0.025 to 0.05 mcg/kg/minute)
  - Maximum dose rage in refractory shock: 35 to 100 mcg/minute (0.5 to 0.75 mcg/kg/minute)
  - If norepinephrine is not available adrenaline or dopamine can be used.
  - If refractory to vasopressor: add hydrocortisone.
  - Hydrocortisone 50mg IV QID or 100mg IV TID.
  - Packed RBC transfusion: if hemoglobin is <7g/dl

- **De-escalation fluids and vasopressors**
  - Patients who respond to therapy: IV fluid administration should be reduced or stopped; vasopressor support weaned
  - If there is sign of fluid overload diuretics should be administered.

- **Empiric antibiotic selection**
  - Broad spectrum IV antibiotic within 60 minutes
  - Empiric antibiotic selection depends on the site of infection, community or hospital acquired, exposure to antibiotics in the last 90 days, comorbidities, local resistance patterns
  - Once culture results are available, revise the antibiotics.
  - See the table below for guidance on community acquired sepsis. For hospital acquired sepsis, see section on hospital acquired pneumonia.

Table 8.52: Empiric antibiotic selection options for community acquired sepsis

(No healthcare admission in previous 90 days and immune-competent patients)

Source	First choice antibiotic regimen	Second line antibiotic
Undifferentiated (no obvious source identified)	Ceftriaxone (Wa): 1 – 2 g IV q 24 hours	
Pneumonia	Ceftriaxone (Wa) 1 – 2g IV q 24 hours + Azithromycin (Wa) Day 1: 500 mg; then 250 mg/day for 4 consecutive days; Add Vancomycin (Wa), if necrotizing pneumonia or high risk of MRSA: Vancomycin 1g IV q 12 hours	Ceftriaxone + Doxycycline (A)
Urinary Tract Infection	Ciprofloxacin (Wa) 500 po q12h or 400mg IV q12h	Ampicillin + Gentamycin
Intra-abdominal Infection	Ceftriaxone 1 – 2g IV q 24 hours + Metronidazole (A) 500mg IV q8h	Amoxicillin-clavulanic acid (A) or Ampicillin-Sulbactam
Skin/Skin Structure Infection – Pure cellulitis	Cefazolin (A) IV1 - 2g IV q 8 hours Add Vancomycin if necrotizing abscesses or high risk of MRSA	Antistaphylococcal penicillin's (e.g cloxacillin)
Skin/Skin Structure Infection with Special Risks	Piperacillin-Tazobactam (Re) 4.5g IV q 8 hours Add Vancomycin (Wa) if necrotizing abscesses or high risk of MRSA	Ampicillin-Sulbactam
Bacterial Meningitis – "Spontaneous"	Ceftriaxone (Wa) 1 – 2g IV q 12h Add Vancomycin (Wa) if gram positive cocci seen in CSF gram stain Add Ampicillin (A) for age < 1 month and > 50 years/immune-compromised	Ampicillin or benzyl penicillin alone (if microorganism identified) or with gentamycin
A: access, Wa: watch and Re: reserve group antibiotic classification, WHO Aware database		

- **Infection source control: within 6 to 12 hours**
- Sepsis control won't be effective if localized abscesses are not drained, foreign bodies or necrotic tissues are not removed.

Table 8.53: Examples of source control methods for common infections

Source	Interventions
Urinary tract focus	Relief of obstruction, removal or changing of infected catheters
Central line (Catheter-related)	Removal of catheter
Soft tissue infection	Debridement of necrotic tissue and drainage of discrete abscesses
Septic arthritis	Joint drainage and debridement
Prosthetic device infection	Device removal
Empyema	Drainage, decortication
Sinusitis	Surgical decompression of the sinuses
Cholangitis	Bile duct decompression

FURTHER READING

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2. J Varon and R M. Baron. A current appraisal of evidence for the approach to sepsis and septic shock. Ther Adv Infectious Dis 2019, Vol. 6: 1–14
3. Rhodes A, Evans LE, Alhazzani W, et al (2017). Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med; 45:304.

8.17 URINARY TRACT INFECTION

BRIEF DESCRIPTION

- Urinary Tract Infection (UTI) refers to the presence of microorganisms in higher numbers to cause invasion of the urinary tract (UT) epithelium and inflammation that cannot be accounted for contamination.
- UTI is classified in different ways that have implication to treatment and outcome

ACCORDING TO ANATOMIC SITE OF INVOLVEMENT:

- Lower UTI: cystitis, urethritis
- Upper UTI: pyelonephritis

ACCORDING TO THE PRESENCE OF STRUCTURAL URINARY TRACT PROBLEMS

- **Uncomplicated UTI**: UTI that occurs in individuals with no structural or functional abnormalities in the urinary tract that interfere with the normal flow of urine.
    - Typically, in women
- **Complicated UTI**: UTI that occurs in individuals with structural or functional abnormalities in the urinary tract.
    - E.g., congenital distortion, obstructive stone, indwelling catheter, vesicoureteral reflux, prostatic hypertrophy, or neurologic bladder.
    - UTI in men should be considered complicated unless proven otherwise.
    - UTI in patients with recent urinary tract instrumentation, postoperative UTI, in patients with kidney transplantation should be considered complicated.
- **Catheter associated UTI:** UTI occurring in a person whose urinary tract is currently catheterized or has been catheterized within the past 48 hours.
    - **Urosepsis** is defined as life threatening organ dysfunction caused by a

body's response to infection originating from the urinary tract or male genital organs.

- ○ **Recurrent UTI-** symptomatic and culture-proven UTI occurring two or more times in six months or three or more times in a year. Recurrent UTI is not necessarily complicated.
- ○ **Asymptomatic bacteriuria:** Bacteiruria > 105 bacteria/ml of urine without symptoms.
- ○ **Symptomatic abacteriuria:** Symptoms of urinary frequency and dysuria in the absence of significant bacteriuria in urine culture.

The presence of pyuria (≥10 WBC/mm^3 of uncentrifuged urine) alone is not sufficient for diagnosis of UTI or bacteriuria. More than 60% of samples in women with asymptomatic pyuria have no bacteriuria.

ETIOLOGIC AGENTS

- Uncomplicated UTI: *Escherichia coli* is the commonest pathogen.
- Complicated or hospital acquired UTI: In addition to *E. coli*, *pseudomonas*, *klebsiella*, *enterobacteria*, *proteus*, *serratia* and assume greater importance.

CLINICAL FEATURES

- **Lower UTI (Cystitis)**
  - ○ Dysuria, frequent urination and urgency
  - ○ Occasionally, gross hematuria
  - ○ Suprapubic pain
  - ○ Elderly people may have nonspecific symptoms: urinary incontinence chronic, malaise, abdominal pain and decreased eating or drinking)
  - ○ N.B: cloudy or malodorous urine are nonspecific features that should not routinely swift for cystitis evaluation OR treatment.
- **Upper UTI (pyelonephritis)**
  - ○ Flank pain

  - Fever, chills and rigors
  - Vomiting
  - Significant costovertebral angle tenderness
  - If associated cystitis (lower UTI), not always present: dysuria, urgency, frequency
  - In elderly: fever or poor feeding or disorientation without another sign
- **Acute prostatitis**: acutely ill, fever, chills, malaise, myalgia, dysuria, frequency, urgency, urge incontinence), pelvic or perineal pain, and cloudy urine.
- **Chronic prostatitis:** usually, symptoms of recurrent UTI (frequency, dysuria, urgency0 perineal discomfort, a low-grade fever, with repeated isolation of the same organism from the urine

INVESTIGATIONS AND DIAGNOSIS

Investigation

- Urinalysis
  - Microscopy for WBC, RBC
  - Dipstick: leukocyte, nitrite
- Urine culture: clean catch mid-stream urine specimen
- CBC
- RFT
- Ultrasound kidneys and prostate (in men 40 years): If complicated only

DIAGNOSIS

- The diagnosis is based on clinical findings plus urinalysis
- Urine analysis
  - Pyuria (WBC > 10 cells/mm3) is present in almost all patients with UTI
- Urine culture:

  - Significant bacteriuria = presence of 105 bacteria (CFU) /ml of urine
  - In symptomatic UTI a lower bacterial count should still be considered positive
  - The diagnosis of recurrent UTI requires culture confirmation
- Digital rectal examination (DRE): For men suspected of having prostatitis; tender or swollen/edematous prostate.
- Ultrasound: when complicated UTI is suspected.

TREATMENT OBJECTIVES

- Eradicate infection and improve quality of life
- Prevent recurrence

Non pharmacologic

- Recurrent UTI: Postcoital voiding, avoiding spermicide use and liberal fluid intake
- Complicated UTI: correction of the underling anatomical or functional abnormality. This requires urologic/gynecologic consultation.

Pharmacologic

A. Acute, Uncomplicated UTI in women

Table 8.54: Antimicrobial regimen selection for urinary tract infections for adults

Scenario	First line options	Alternatives
Acute uncomplicated UTI (cystitis) in women	Ciprofloxacin 250- 500mg PO, BID or Norfloxacin, 400mg PO., BID, for 3 days. OR Nitrofurantoin 50mg P.O., QID for 5 days (effective if available) OR Cotrimoxazole (TMP-SMO) 160/800mg P.O, BID for 3 days (Only if the local resistance is known to be <20%)	Fosfomycin 3g single dose OR Cefpodoxime100mg PO, BID for 5 days *OR* Amoxicillin-clavulanate 500/125mg TID for 5 days
Uncomplicated mild to moderate pyelonephritis (Mild to moderate): able to take orally, no vomiting, no dehydration, no sepsis)	Ciprofloxacin, 500mg P.O., BID, oral for 7-10 days.	Cefpodoxime, 200mg P.O., BID for 10 days preceded by a single dose of ceftriaxone 1gm IV/IM.
Severe pyelonephritis *vomiting, dehydration, or evidence of sepsis)* without risk of resistant infections– *start IV*	Ciprofloxacin, 400mg, IV, BID. Complete 10-14 days with oral Ciprofloxacin 500mg BID at discharge OR Ceftriaxone, 1- 2gm, IV, daily, followed by oral ciprofloxacin. OR Cefotaxime 1gm IV TID, followed by oral ciprofloxacin	If no response to these options within 48- 72 hours, use options listed in the category (sever pyelonephritis with risk of resistant pathogens)

Severe pyelonephritis with the either of following three risk factors for of resistant pathogens in the last 3 months 1. Multidrug-resistant urinary isolate 2. Inpatient stay at a health care facility 3. Use of a broad-spectrum antibiotic (fluoroquinolone, third or later generation cephalosporin trimethoprim-sulfamethoxazole)	Meropenem 1gm IV TID OR Imipenem 500mg IV QID	OR Cefepime 2 gm IV TID OR Ceftazidime 2 gm IV TID OR Piperacillin-tazobactam 3.375 gm IV QID Addition of aminoglycoside: Gentamycin 3-5mg/Kg, IV, once daily can be sonsidered.

RECURRENT UTI

- Antibiotic prophylaxis is recommended for women who experience two or more symptomatic UTIs within six months or three or more over 12 months.
- The degree of discomfort experienced by the woman needs to be considered in the decision.
- Recurrent pyelonephritis deserves prophylaxis.
- Any prophylaxis should be given after current active infection is treated.
- Prophylaxis regimen options
  - Continuous: daily (sometimes three times per week)
  - Postcoital: a single dose of antibiotic after every sexual activity; if there is clear temporal relationship between episodes of the recurrent UTI and sexual intercourse.

  - Self-treatment (Not actual prophylaxis): A 3 days short course treatment in a patient who clearly understand the symptoms. To be started at the first onset of symptoms. Risk of recurrence remains high.

- **The antibiotic prophylaxis options**
  - **Trimethoprim-sulfamethoxazole** 40 mg/200 mg once daily or 3 times per week
  - **Nitrofurantoin** 50 mg or 100mg once daily
  - **Cefaclor** 250 mg once daily
  - **Cephalexin** 125 mg -250mg once daily
  - **Norfloxacin** 200 mg once daily
  - **Ciprofloxacin** 125 mg once daily

PROSTATITIS

- **Acute bacterial Prostatitis**: Floroquinolones or Trimethoprim/ sulfamethoxazole is first line agent. Duration of treatment is 4 weeks (28 days).
- **Chronic bacterial prostatitis:** Difficult to treat. Similar antibiotics to acute bacterial are use but for a duration of 1–4 months.

ASYMPTOMATIC BACTERIURIA

- It should not be treated with antibiotics.
- The only two indications to treat with antibiotics: pregnancy and prior to invasion urinary tract instrumentation.

PREGNANCY AND UTI

- Antibiotics to be avoided for pregnant women: fluoroquinolones, aminoglycosides and trimethoprim/sulfamethoxazole
- Antibiotics recommended for uncomplicated UTI in pregnant women: amoxicillin/clavulanate, cephalexin or cefpodoxime for 3-5 days
- Antibiotics recommended for severe or complicated scenarios: third generation cephalosporin's (cefotaxime or ceftriaxone).

- In the presence of a risk for resistant infections: carbapenems, piperacillin-tazobactam or cefepime or ceftazidime.

FURTHER READING

1. G. Bonkat (Chair), R. Bartoletti, F. Bruyère et al. European Association of Urology guidelines: Urological Infections - Limited Update March 2020.
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8.18 INTESTINAL HELMINTHIC INFESTATIONS

BRIEF DESCRIPTION

- These are infestation caused by intestinal worms (nematodes and cestodes), which are commonly associated with poor personal and environmental hygiene.
- Although they may not be fatal, they contribute to malnutrition and diminished work capacity.

CLINICAL FEATURES

- Include abdominal cramps, nausea, bloating, anorexia
- Anemia
- Perianal itching
- Passage of adult worms

INVESTIGATIONS

- Mainly by direct stool microscopy: A single stool microscopy may not be diagnostic. A repeated stool microscopy may be needed.

TREATMENT

OBJECTIVES

- Reduce symptoms
- Break the cycle of transmission

Pharmacologic (See table below)

Table 8.55: Treatment of common intestinal helminthic parasitic infestations

Name of infestation Etiology Mode of transmission	Treatment	Remark
Ascariasis ***Ascaris lambricoids*** Ingestion of the larvae of the parasite together with food	**First line-options** **Albendazole,** 400mg P.O. as a single dose, for children: 1 – 2 years, 200mg as a single dose. **Mebendazole,** 100mg P.O.BID for 3 days or 500mg, once **Alternative (pregnant women)** **Pyrantel pamoate**, 700mg P.O. as a single dose	Presence of migrating larvae in the lungs can provoke pneumonia

Enterobiasis ***Enterobius Vermicularis*** Ingestion of the eggs of the parasite together with food	**First line-options** **Mebendazole,** 100mg P.O. BID for 3 days, repeat in two weeks OR **Albendazole,** 400mg P.O. as a single dose, repeat in two weeks, Alternative **Piperazine,** 4g in a single dose. • Simultaneous treatment of the entire household is warranted due to high transmission possibilities	Common in children and auto infection may occur
Hookworm infestation *Necator americanus or Ancylostoma duodenale* Penetration of the larvae of the parasite through skin	**First line-options** **Albendazole,** 400mg P.O. as a single dose (**preferred**) OR **Mebendazole,** 100mg P.O. BID for 3 days or 500mg stat **Alternatives:** **Pyrantel pamoate**, 700mg P.O. as a single dose	

Strongyloidiasis ***Strongloidexs stercolaries*** Penetration of the larvae of the parasite through skin	**First line** **Ivermectin,** 200mcg/kg daily for 2 days. For disseminated strongyloidiasis, treatment with ivermectin should be extended for at least 5–7 days or until the parasites are eradicated. **Alternatives-**options **Albendazol**e 400mg P.O.BID for three consecutive days (less effective than ivermctin). OR **Thiabendazole,** 1500mg, P.O. BID, for children: 25mg/kg p.o. for three consecutive days (comparable efficacy to ivermectin).	Larvae migrate to the lungs where they cause tissue destruction and bleeding. Treat concomitant anemia if any
Trichuriasis ***T.tricura***	**First line-options** **Mebendazole**, 500mg P.O., single dose **(preferred over Albendazole)** OR **Albendazole,** 400mg, P.O. for three days oxantel pamoate 15 to 30 mg/kg (if available) plus albendazole 400 mg on consecutive days is superior than other therapies	Heavy infestation leads to bloody diarrhea, bleeding & weakness

Taeniasis ***T.saginata*** ***T.solium***	**First line-Intestinal infestation** **Praziquantel** P.O. 600mg or 10mg/Kg, single dose **Alternative** **Niclosamide,** 2g in a single dose P.O. **Treatment of neurocysticercosis** **Albendazole** P.O. 15mg/kg per day for 8- 28 days **or** **Praziquantel** 50–100mg/kg daily in three divided doses for 15–30 days. Longer courses are often needed in patients with multiple subarachnoid cysticerci **PLUS** -High-dose glucocorticoids -Anti epileptics (if there is seizure)	*T. solium* (pork tapeworm) may cause fatal cysticercosis
Hymenolepis nana	**First line** **Praziquantel**, 25mg/kg or 1800mg P.O. single dose, followed by repeat dose 10 days later **Alternatives** **Niclosamide,** 2g P.O. on the first day followed by 1g QD for 6 days	

8.19 BRUCELLOSIS

BRIEF DESCRIPTION

- Brucellosis is a zoonotic infection caused by different species of the gram-negative bacteria, *Brucella species*. *B. melitensis* is the most virulent and invasive.
- Transmission to humans occurs through direct contact, through broken skin, with infected animal tissue, inhalation of infectious aerosols, or ingestion of infectious milk or dairy products from infected animals (sheep, cattle, goats, pigs, or other animals)
- Sporadic cases and sometimes large outbreaks occur after consumption of raw milk and milk products.
- Brucellosis is endemic in Ethiopia.
- A seroprevalence study among healthy blood donors in southern Ethiopia found a prevalence of 10.6%.
- Clinical brucellosis is a systemic disease with a broad spectrum of presentation ranging from asymptomatic to severe or fatal illness
- The main presentations are acute febrile illness, with or without signs of localization, and chronic infection

CLINICAL FEATURES

Acute brucellosis

- Insidious onset of fever and night sweats (with a strong, peculiar, moldy odor)
- Arthralgia, myalgia, low back pain, headache, dizziness
- Anorexia, weight loss
- Fatigue, malaise
- Dyspepsia, abdominal pain
- cough

- Hepatomegaly, splenomegaly, lymphadenopathy may be observed.

LOCALIZED INFECTION: brucellosis can affect any organ system

- Osteoarticular: the most common presentation.
    - The sacroiliac joints and large joints of the lower limbs are most frequently involved
    - Spondylitis: Lumbar more than the thoracic or cervical vertebrae. Paravertebral, epidural, and psoas abscess can be present.
- Genitourinary: orchitis/epididymitis, prostatitis, cystitis, or tubo-ovarian abscess
- Pulmonary: Bronchitis, interstitial pneumonitis, lobar pneumonia, lung nodules
- Cardiovascular: endocarditis
- Gastrointestinal: hepatitis
- Hematological: anemia, leukopenia, thrombocytopenia, pancytopenia
- Neurological: meningitis (acute or chronic), encephalitis, myelitis, radiculitis,
- Dermatologic: macular, maculopapular, scarlatiniform, papulonodular, and erythema nodosum-like eruptions
- Ocular involvement: commonly presents with uveitis.

CHRONIC BRUCELLOSIS:

- Refers to brucellosis with clinical manifestations for more than one year after the diagnosis
- It is characterized by localized infection (generally spondylitis, osteomyelitis, abscesses, or uveitis) and/or relapse with objective evidence of infection (elevated antibody titers and/or recovery of brucella from blood or tissues).

Relapse

- Relapse usually occurs within six months after treatment.

INVESTIGATIONS AND DIAGNOSIS

- High index suspicion needed for diagnosis. Many of the clinical manifestations are similar to tuberculosis

The following laboratory tests are used to support or confirm the diagnosis:

- Isolation of Brucella from blood, bone marrow, pus, or other tissues:
  - Blood culture – requires special technique and long incubation period, and is often negative in long-standing disease
  - PCR for Brucella: Not Routinely available
  - Both of the tests above are not widely available in Ethiopia
- Serological tests for Brucella antibodies in blood or other tissue:
  - Combine Rose Bengal test for agglutinating antibodies (IgM, IgG, IgA) with a test for non-agglutinating antibodies
  - IGG (ELISA-IgG). Antibody Titers of 1:160 or higher are very highly suggestive of the diagnosis of brucellosis
- X-rays to demonstrate joint disease (blurred joint margins, widened sacroiliac space, destruction of vertebrae)

TREATMENT

OBJECTIVES

- Control and eradicate the infection
- Prevent complications, relapses, and sequelae

NON PHARMACOLOGIC

- Surgical intervention e.g., abscess drainage, joint replacement will be needed for focal infections

Pharmacologic

The general principle for brucellosis treatment includes:

- Use antibiotics having activity in acidic cellular environment (e.g., doxycycline & rifampin)

- Use two or more antibiotics in combination for success (high relapse with monotherapy)
- Prolonged duration of treatment.
- Treatment depends on the presence or absence of focal disease

Table 8.56: Treatment of brucellosis for non-pregnant adults and ≥8 years old children

	First line	Alternatives
No focal Disease	**Doxycycline**, for 6weeks PLUS **Gentamycin** for the first 7days or **Streptomycin** for 14-21 days	**Doxycycline** for 6weeks *PLUS* **Rifampicin** for 6 weeks The relapse rate is 10-20%.
Spondylitis (sacroiliitis, peripheral arthritis)	**Doxycycline** for at least12 weeks PLUS **Gentamycin** for 14 days PLUS **Rifampcin** for 12 at least 12 weeks	**Ciprofloxacin**, for at least 3months, **PLUS** **Rifampicin**, for at least 3months
Neurobrucellosis	**Ceftriaxone** for 4 - 6 weeks PLUS **Rifampin and doxycycline** for at least 12 weeks	**Doxycycline** *PLUS* **Rifampicin &Sulphamethoxazole-Trimethoprim** for at least 12 weeks
Endocarditis	**Gentamicin** for 14 days PLUS Rifampin and doxycycline for at least 12 weeks	Surgery may be required.

Table 8.57: Doses of antimicrobials used in the treatment of brucellosis

Drugs	Adult Dosing	Pediatric dosing
Doxycycline	100 mg orally twice daily	4.4 mg/kg per day (maximum 200 mg/day) orally in 2 divided doses for 6 weeks
Streptomycin	1 g intramuscularly or intravenously once daily	15 to 40 mg/kg per day (maximum 1 g/day) intramuscularly or intravenously in 1 to 2 doses
Gentamicin	5 mg/kg/day intramuscularly or intravenously in 1 dose	5 mg/kg/day intramuscularly or intravenously in 1 dose
Rifampin	600 to 900 mg orally once daily	15 to 20 mg/kg per day (maximum 900 mg/day) orally once daily
TMP-SMX	1 double-strength tablet orally twice daily	TMP 10 mg/kg per day (maximum 320 mg/day) and SMX 50 mg/kg per day (maximum 1.6 g/day) divided in 2 doses
Ceftriaxone	2 g intravenously once daily	100 mg/kg/day divided every 12 hours (maximum 2 g per dose)
Ciprofloxacin	750mg P.O., BID	

PREVENTION

- Tools for prevention of brucellosis include:
    - ○ Avoiding consumption of raw milk (consume boiled or pasteurized)
    - ○ Precautions for individuals at risk for occupational exposure
    - ○ Control of the disease in animals (regular animal vaccination).
    - ○ Screening household members of an index case
    - ○ Postexposure prophylaxis (PEP): for laboratory personnel in contact with a culture positive specimen.

  - No vaccines for brucellosis in humans

SPECIAL POPULATION CONSIDERATIONS

- **Pediatrics and pregnant women**: Doxycycline should not be used in children < 8 years and pregnant women. Trimethoprim – sulfamethoxazole should be used in place of doxycycline for all the above regimens. If ≥ 36 weeks of gestation Trimethoprim – sulfamethoxazole should be avoided.

FURTHER READING

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2. M.J. Corbel. Brucellosis in humans and animals. WHO/CDS/EPR/2006.7. World Health Organization 2006.

8.20 ANTHRAX

BRIEF DESCRIPTION

- Anthrax is an infection caused by a bacterium called B. *anthracis*, a gram-positive, rod- shaped bacteria that exists in the environment as a spore and can remain viable in the soil for decades.
- Spores ingested by grazing herbivores germinate within the animal to produce the virulent vegetative forms that replicate and eventually kill the host.
- Products (e.g., meat or hides) from infected animals serve as a reservoir for human disease.
- B. anthracis can invade the human body by transcutaneous, gastrointestinal, and pulmonary routes
- Infection can lead to localized or systemic disease:
  - Cutaneous anthrax: when spores enter cutaneous, they become vegetative, multiply, locally spread, and produces toxins which cause extensive edema and tissue necrosis.

- Gastrointestinal anthrax follows ingestion of contaminated and undercooked meat.
- Inhalational anthrax: spores enter alveoli, cause hemorrhagic mediastinitis. Left untreated it is universally fatal.

CLINICAL FEATURES

- **Cutaneous anthrax:** eschar with extensive surrounding edema is the hallmark
  - Most common form
  - Lesions occur in exposed areas: face, neck, arms, and hands.
  - Starts as small, painless, pruritic papule
  - A ring of vesicles develops around the papule.
  - Vesicular fluid may be exuded
  - The original papule ulcerates with a necrotic a black, depressed eschar (dead tissue)
  - Extensive edema of the surrounding tissues
  - Regional lymphadenopathy and lymphedema
  - Edema with face or neck infection may produce airway compromise.
- **Gastrointestinal anthrax**
  - Initial symptoms: headache, low-grade fevers, and conjunctival injection.
  - Oropharyngeal: sore throat, dysphagia and painful regional lymphadenopathy. Extensive swelling of the neck and chest wall.
  - Gastrointestinal: Abdominal pain, nausea/vomiting, less frequently diarrhea. Progressive ascites and hypotension.
- **Inhalational anthrax**
  - Initial phase (4-5 days): myalgia, fever, and malaise, hemoptysis, dyspnea, odynophagia, or chest pain

  - Fulminant bacteremic phase: progressive severe dyspnea, hypoxia, and shock.
- **Meningitis:** can occur in association with any of the other forms of anthrax.
  - Typically, hemorrhagic meningitis: hemorrhagic CSF confusing with traumatic LP.
  - Delirium or coma, seizures, cranial nerve palsies, myoclonus

INVESTIGATIONS AND DIAGNOSIS

- A high index of suspicion is needed in those who have exposure to animals.
- Specimen for gram stain and culture
  - Swab from cutaneous lesion: unruptured vesicles, base of ulcer, eschar (elevate the edge and swab the base)
  - Oropharyngeal lesion
  - Pleural fluid, ascitic fluid should be sampled if present
  - In GI anthrax: stool, rectal swab
  - Blood culture
  - All patients with suspected systemic anthrax or meningitis should have lumbar puncture unless contraindicated.

TREATMENT

OBJECTIVES

- Clear the bacteria
- Decrease toxin production and spread
- Decrease morbidity and mortality

Non pharmacologic

- Apply contact isolation precautions for patients with draining anthrax lesions.

- Drain pleural fluid: Chest tube drainage, improves survival by decreasing toxin level
- Drain ascites: drain as much as possible (continuous or frequent intermittent drainage)
- Standard sepsis care: IV fluids for patients with systemic anthrax.
- Other supportive cares

Pharmacologic

- **Antimicrobial therapy**

Table 8.58: Antimicrobial therapy for anthrax

	First line	Alternative	Duration
Anthrax with meningitis **OR** **Systemic anthrax when meningitis is not ruled out by CSF analysis**	Ciprofloxacin 400 mg IV TID PLUS Meropenem 2g IV TID PLUS Clindamycin 900mg IV TID	• If Meropenem or other carbapenems are not available, replace it with Penicillin G 4million IU Q4hr OR Ampicillin 3gm Q 6hr • If clindamycin is not available replace it with either Rifampicin 600mg BID OR Chloramphenicol 1gm Q6hr	At least 2 weeks or until the patient is clinically stable, whichever is longer. Complete a 60-day course with either of the following two oral agents Ciprofloxacin 500mg BID OR Doxycycline 100mg BID

Systemic anthrax when meningitis is excluded	Ciprofloxacin 400 mg IV TID PLUS Clindamycin 900mg IV TID	• If clindamycin is not available replace it with either Doxycycline 200mg loading, then 100mg BID OR Chloramphenicol 1gm Q6hr	Similar to meningitis: see above
Cutaneous anthrax with no systemic involvement	Ciprofloxacin 500mg PO BID OR Doxycycline 100mg PO BID	Clindamycin 600mg PO TID	7-10 days
Considerations for special population All the considerations above are applicable for pregnant, lactating, and postpartum women. However, ciprofloxacin is strongly preferred when single agent is used.			

- **Corticosteroids:** Hydrocortisone or Dexamethasone IV
    - Indications: meningitis, extension head and neck edema in cutaneous anthrax, vasopressor refractory shock
- **Antitoxin therapy:** is recommended for patients with systemic anthrax. Anthrax immunoglobin derived from human plasma can be used for this purpose.

PREVENTION

- Annual vaccination of livestock is the major means of preventing naturally occurring epizootics of anthrax.
- Pre-exposure vaccination with anthrax vaccine adsorbed (AVA) for likely

occupational exposure to aerosolized Bacillus anthracis spores.

- Post-exposure prophylaxis (PEP) for documented or suspected inhalational anthrax with oral single antimicrobial agent (ciprofloxacin preferred) (doxycycline can be used for non-pregnants') for 42 to 60 days plus vaccination.
- For naturally occurring gastrointestinal or cutaneous antimicrobial prophylaxis a 7- to 14-day ciprofloxacin may be considered but no vaccination is recommended

FURTHER READING

1. Anthrax in humans and animals Fourth edition. World health organization 2008. ISBN 978 92 4 154753 6
2. Kamal SM , Rashid AKM M , Bakar MA et al. Anthrax: an update. Asian Pac J Trop Biomed 2011; 1(6): 496-501.

8.21 LEISHMANIASIS

OVERVIEW ON LEISHMANIASIS

- Leishmaniasis is a disease caused by protozoa, which belong to the genus *Leishmania*.
- The transmission of Leishmaniasis is either **zoonotic**, which includes animal reservoir hosts, mainly dogs, in the transmission cycle, or **anthroponotic** in which humans are the sole source of infection for the vector
- It is transmitted either from humans to humans or animal to humans by the bite of phlebotomine sand flies.
- It has two major clinical forms: **cutaneous** and **visceral leishmaniasis** (also called Kala azar).
- Another clinical and public health wise important entity is post kala azar dermal leishmaniasis (PKDL).
- PKDL occurs in patients with visceral leishmaniasis towards the end or shortly after treatment. The skin lesions harbor the Leishmania parasite

and they are potential source of transmission.

- In Ethiopia, both the cutaneous and visceral forms of Leishmaniasis are endemic. However, these two diseases are caused by different species, transmitted differently and occur in different localities.
- Transmission of visceral Leishmaniasis in Ethiopia is human to human while that of cutaneous is zoontic.
- Visceral Leishmaniasis is mainly found in the lowlands of northwest, central, south and southwestern Ethiopia; whereas cutaneous Leishmaniasis is widely distributed all over the country.
- Several outbreaks of Visceral Leishmaniasis have occurred in Ethiopia. The disease is spreading to new localities due to population movement and HIV co-infection.
- It is estimated that the annual burden of Visceral Leishmaniasis in Ethiopia ranges from 2,000 to 4,500 cases.

8.21.1 VISCERAL LEISHMANIASIS (KALA AZAR)

BRIEF DESCRIPTION

- Symptomatic visceral Leishmaniasis (VL) (*kala azar)* is a life-threatening disease.
- In Ethiopia VL is caused by *L. donovani* through an anthroponotic (Human-Sandfly-Human) transmission.
- A significant proportion of infected individuals may be asymptomatic.
- The incubation period is typically 2–6 months, but it can also last to few years. Clinical manifestation.
- History of residence to endemic areas or travel history is important when considering VL in a patient. It is also important to note the epidemiology of VL in Ethiopia is every changing, with new endemic areas being found.

CLINICAL FEATURES

- Fever
- Progressive weight loos
- Loss of appetite, fatigue
- Left upper abdomen fullness or dragging sensation
- Recent treatment for bacterial infections e.g., pneumonia, otitis media
- Pallor
- Splenomegaly: usually massive
- Hepatomegaly: Less marked than splenomegaly
- Lymphadenopathy: occasionally found
- Advanced VL: cachexia, hypoalbuminemia, edema, ascites, jaundice, hepatic dysfunction
- HIV co-infection may alter the clinical presentation: atypical sites (non-reticuloendothelial) tend to be more involved. Oral mucosa, gastrointestinal and diffuse skin involvement (at the same time with the VL)

Investigations and diagnosis

- Investigations: CBC, blood film of malaria, LFT, RFT, serum albumin and total protein

DIAGNOSIS

- **Clinical case definition**: Although the clinical definition of VL is not specific, patients fulfilling the case it should have either parasitologic and/or immunologic tests for designed for the diagnosis.

Clinical case definition of VL: A person who lives in VL endemic area or having travelled to an endemic area presenting with fever for more than two weeks after exclusion of malaria or treating for malaria and one or more of the followings

1. Splenomegaly (with or without lymphadenopathy)
2. Weight loss
3. Cytopenia: anemia or leucopenia or bi/pancytopenia

- A confirmation of the diagnosis requires identification of the parasite.
- Although they have limitations, immunologic tests are also helpful in diagnosis.
- Parasitologic confirmation: detection of the amastigote stage of the parasite
    - Specimen:
        - Splenic aspirate: it is the preferred specimen; has the highest yield (sensitivity of 93-99%). It should be by an experienced trained person and be avoided in patients with low platelet count, coagulopathy or active bleeding due the risk of splenic hemorrhage which could be fatal.
        - Bone aspirate: safe, variable but reasonable sensitivity (53-86%)
        - Lymph node aspirate: safe, relatively low sensitivity (53-65%)
    - Staining: Giemsa
    - The Amastigote (LD body): small spherical or ovoid shaped structures with prominent nucleus and deeply stained rod-like structure in the cytoplasm (called kinetoplast).They could be found within macrophages or extracellularly.
- Immunologic tests
- Antibody detection tests
    - Limitations
        - They cannot differentiate between present and past infections.
        - They cannot be used to for diagnosis of relapses is not possible.
        - Asymptomatic individuals living in endemic areas can be positive.
    - Can be used when parasitologic diagnosis is not possible or negative (with high index clinical suspicion)
    - Available test (extensively evaluated): DAT (Direct agglutination test) and rK39.The rK39 test is available in a rapid test format (rK39 dipstick).

- **Antigen Detection Test**
    - A urine latex agglutination (KATEX) that detects antigen of the parasite.
    - It is more specific but less sensitive than the antibody test
    - It helps to distinguish active from past infections

- **Primary VL case:** A patient who is diagnosed with VL for the first time
- **Initial cure**: Absence of symptoms and signs at the end of treatment for VL. If there is no resolution of the clinical and laboratory parameters parasitologic test is needed.
- **Definitive cure:** initial cure PLUS and a negative parasitologic test (test of cure, TOC) after 6 months of treatment.
    - Unless there is suspicion of relapse, test of cure should be done routinely.
- **Relapse VL case:** If a patient returns with clinical features and a positive parasitologic test for VL, after having successful treatment of primary VL and discharged improved or with a negative test of cure.

TREATMENT

OBJECTIVES

- Reduce the parasite burden
- Deceases toxicity of medications
- Prevent development of resistance
- Improve the clinical outcome (decrease morbidity and mortality)

Non pharmacologic

- Nutritional support
- Transfusion: if indicated (packed RBC, platelets)
- Evaluation and treatment of other infections

Pharmacologic

<table>
<tr><th>First line therapy for primary VL</th><th>Preferred therapy primary VL in special situations</th><th>Treatment options for first VL relapse</th></tr>
<tr><td>Sodium Stibogluconate (SSG) 20mg/kg body weight/day IM daily x 17 days
PLUS
Paromomycin (PM) 15mg/kg body weight/day IM daily for 17days
If Paromomycin is not available the first line therapy:
Sodium stibogluconate, 20 mg/Kg/day given IV (slow infusion over at least 5min) OR IM in a single daily dose X 30 days</td><td><u>Special situations</u>
• Pregnancy
• HIV- coinfection
• Severe illness (Clinical)
• Severe anemia
• Severe malnutrition
• Age < 2 or >45 years
• Severe toxicity from sodium stibogluconate requiring interruption
Liposomal amphotericin B (AmBisome) 5mg/kg/day X 6days</td><td>If possible, the regimen used for the treatment of relapses should be a different from the one used in primary VL.
Options
Liposomal amphotericin B 5mg/kg/day for a period of 6 days.
OR
SSG 20 mg/kg/day for 40days, with 2 consecutive weekly aspirates for parasite being negative.
If the test of cure is still positive, SSG should be given for a total of 60 days
OR
SSG/Paromomycin combination:
SSG (30 days) PLUS Paromomycin (17 days)</td></tr>
<tr><td colspan="3">Alternative: Miltefosine 2-3mg/kg /day (100mg/day for anyone weighing > 25kg) for 28 days. Miltefosine is an oral drug which can be used as an alternative in non-pregnant, non-HIV patients if SSG is not tolerated.</td></tr>
<tr><td colspan="3">Treatment of PKDL: mild forms do not need treatment. For those with non-mild disease. The options are: SSG 20mg/kg/day for 30 days OR Miltefosine 2-3mg/kg /day (100mg/day for all >2kg 25kg) for 28 days.</td></tr>
</table>

ADVERSE EFFECT MONITORING

SODIUM STIBOGLUCONATE (SSG)

- The most serious adverse effects of SSG: cardiotoxicity and clinical pancreatitis.
- Other frequent side effects of SSG: myalgia and arthralgia, nausea, vomiting, rash, nonspecific ECG abnormalities, elevated liver function tests, elevated lipase and amylase levels, and cytopenia (leucopenia, anemia, thrombocytopenia or combination).
- Monitoring (Baseline and weekly while on treatment): clinical monitoring, ECG, CBC, RFT, LFT, amylase and lipase.
- Ominous ECG changes: Prolongation of the corrected QT(QTc) to >0.5 seconds or of T wave inversion with concave ST segments.
- Indications to stop SSG due to adverse effects
    - Clinical acute pancreatitis: abdominal pain and vomiting (elevated amylase or lipase alone without clinical evidence are not enough reasons to stop)
    - Ominous ECG changes: Prolonged QTc or T wave inversion with concave ST segment
    - Significantly elevated liver enzymes (at least 5 times upper normal limit)
    - Jaundice developing while on treatment
    - Acute kidney injury developing while on treatment
    - Refractory severe vomiting
    - Declining hematologic parameters (WBC, Hb or Platelets)

Paromomycin: Adverse effects are uncommon; elevated liver enzymes, reversible ototoxicity, renal insufficiency, and tetany (which are rarely reported).

Liposomal Amphotericin B: Infusion reaction (rigors), renal toxicity (acute kidney injury, hypokalemia, hypomagnesemia, nephrogenic diabetes insipidus). Hydrate patients and monitor RFT and electrolytes.

FURTHER READING

1. Guideline for the diagnosis, treatment and prevention of Leishmaniasis in Ethiopia, 2nd edition, June 2013. Ethiopian Federal Democratic Republic of Ethiopia Ministry of Health.
2. S Burza, S L Croft, and M Boelaert. Leishmaniasis. www.thelancet.com. Published online August 17, 2018. http://dx.doi.org/10.1016/S0140-6736(18)31204-2

8.21.2 CUTANEOUS LEISHMANIASIS (ORIENTAL LEISHMANIASIS, ORIENTAL SORE, LEISHMANIASIS TROPICA)

BRIEF DESCRIPTION

- Cutaneous Leshmaniasis in Ethiopia is caused by *Leishmania tropica or Leishmania aetiopica*, which is transmitted by phlebotomus sand fly.
- Before ulceration occurs, there appears dermal infiltrates consisting of large histiocytes filled with many leishman-donovan (L-D) bodies, while during ulceration an influx of neutrophils occurs. Older lesions develop a tuberculoid infiltrate and at this stage either the organisms are scant or absent.

CLINICAL FEATURES

- Cutaneous leishmaniasis (CL) is a disease of the skin and mucous membranes. There are different clinical forms of CL: localized CL, diffuse CL, and mucosal leishmaniasis. The typical features of each are outlined below.
- **Cutaneous lesions**
    - Occur mainly on exposed body parts (face, neck, arms, legs)
    - May be single or multiple with regional lymph node enlargement
    - Are usually painless
    - If secondarily infected, they can be painful and itchy

- **Localized cutaneous leishmaniasis**
  - Papule at the site of the bite (like an insect bite)
  - If papule persists, it develops into either:
  - A small nodule
  - An ulcer with a flat base and raised border
  - The nodulo-ulcerative form (broad-based ulcer with crust)
  - Leishmaniasis recidivans is localized CL that is characterised by a chronic solitary lesion that expands slowly and often reoccurs. The lesion can continue for many years, causing severe disfigurement.
- **Diffuse cutaneous leishmaniasis**
  - Coalescence of papules and nodules to form plaques
  - Chronic and very difficult to treat
  - Mucosal leishmaniasis
  - It is the most severe form of CL, causing severe disfigurement and mutilation of the face
  - Nasal lesions: discharge, bleeding, obstruction, deformity, and destruction of cartilage with collapse of the nose
  - Oropharyngeal lesions: difficulty chewing and swallowing, bleeding gums, toothache, loose teeth, perforation of the hard palate
  - Involvement of mucosa can follow:
    - Primary infection (with L. major or L. donovani)

      OR
    - Dissemination of cutaneous leishmaniasis

      OR
    - Treatment for visceral leishmaniasis (post-kala-azar dermal leishmaniasis)

INVESTIGATIONS AND DIAGNOSIS

- Diagnosis requires clinical suspicion in individuals living or travelled to endemic areas and demonstration of the parasite form the lesions
- Clinical suspicion
    - **Cutaneous Leishmaniasis**
        - A skin nodule or ulcer with a raised edge appearing on someone who lives in an area known to be endemic for cutaneous Leishmaniasis or visited such an area in the last two years.
    - **Mucocutaneous Leishmaniasis (MCL)**
        - Infiltrative inflammation of the mucocutaneous borders of the nose and/or lips, or swelling and expansion of the nose.
    - **Diffuse Cutaneous Leishmaniasis (DCL)**
        - Resembles lepromatous leprosy, but peripheral nerves, eyes, oronasal mucosa and internal organs are not involved.
- Demonstration of the parasite
    - Microscopic identification of intracellular amastigote in Giemsa-stained specimens from lesions
- Leishmanian skin test and serology tests are of little use in the diagnosis of cutaneous leishmaniasis.

TREATMENT

OBJECTIVES

- Kill the parasite and control its spread,
- Enhance healing, reduce scarring and prevent disfigurement.

Non pharmacologic

- Thermotherapy (1 or 2 applications of localized heat (55°C during 5 minutes) using a thermal device), with or without cryotherapy with liquid nitrogen (-195°C) applied to the lesion once or twice weekly up to 6 weeks.

Pharmacologic

Treatment Options

- There are 3 options for treatment of CL.These options should be discussed with the patient:
  - No treatment
  - Local treatment
  - Treatment with systemic drugs
- The decision depends on the size, nature, and location of the lesions and the ability of the patient treatment follow-up.

No Treatment:

- If patients with CL fulfill all of the following and make informed decision, they can be observed with no treatment. Follow up to re-evaluate the treatment options should be arranged every 3 months.
  - < 2 lesions requiring immediate treatment
  - Lesions < 5 cm in diameter
  - Absence of indurations or firmness of surrounding skin,
  - No mucosal involvement OR lesions are not close to the nose or the lips
  - Lesions are not on the border of the lip, the nostrils or the eyes;
  - No potentially disfiguring or disabling lesion (on the nose, the joints, the toes, or the fingers)
  - No immuno-suppression
- **Local treatment**
  - For few (<3) but large lesions
  - Options
    - Intra-lesional **Sodium stibogluconate (SSG):** weekly for four

to six weeks. It should be given by trained personnel. Evaluate weekly for the need of reinjection.

  - Cry**otherapy**
  - **A combination of intra-lesional SSG and cryotherapy**
  - **Thermal ther**apy (radio waves delivered by a device) under local anesthesia
  - Curettage under local anesthesia

- **Systemic treatment**
  - Indications:
    - Mucocutaneous Leishmaniasis
    - Diffuse cutaneous Leishmaniasis
    - Lesions located over joints
    - Large lesions unsuitable for local treatment
    - More than 4 lesions
    - At risk of mucosal Leishmaniasis (lesions on the margin of the nostril or lip)
    - Lesions which are bothersome to the patient but unsuitable for local treatment
    - Lesions accompanied by nodular lymphangitis
    - Immuno-compromised patients (HIV/AIDS)
    - Patients not responding to topical treatment

First Line

- **Paromomycin**, 14–15mg (sulphate) /kg IM once daily for 20–30 days.

Alternatives

- **SSG** 20mg kg/day IM or IV for 4–8 weeks.

OR

- ○ **Liposomal Amphotericin B** 2-3mg/kg/day (for a total of 20-40mg/kg)

OR

- ○ **Miltefosine** 2-3mg/kg /day (100mg/day for anyone weighing > 25kg) for 28 days

- **Response to Treatment**
  - ○ The signs of therapeutic response or natural healing are flattening followed by re-epithelization of the lesion.
  - ○ Clinical reactivation usually begins at the margins of the old lesions.
  - ○ The response is generally poor in HIV co-infections resulting in high rates of recurrence, treatment failure and relapse.

FURTHER READING

1. Guideline for the diagnosis, treatment and prevention of Leishmaniasis in Ethiopia, 2nd edition, June 2013. Ethiopian Federal Democratic Republic of Ethiopia Ministry of Health.
2. S Burza, S L Croft, and M Boelaert. Leishmaniasis. www.thelancet.com. Published online August 17, 2018. http://dx.doi.org/10.1016/S0140-6736(18)31204-2

8.22 SCHISTOSOMIASIS

BRIEF DESCRIPTION

- Schistosomiasis is a disease caused by trematodes, which include *Schistsoma mansoni*, *Schistsoma japonicum and, Schistsoma haematobium*. The first two species inhabit venules of the intestines whereas the latter are found mostly in the venules of the urinary tract.
- Human infection occurs as a result of penetration of the unbroken skin by the free- swimming cercariae larva. This often occurs in individuals

who have frequent contact with water bodies heavily infested with appropriate snail hosts.

- Schistosomiasis risk is most parts of Ethiopia including urban areas. Some areas are known to be endemic.
- *S. mansoni* is endemic in the Omo, Awash, and Blue Nile River valleys.
- *S. haematobium* is also present, specifically in the lower Awash Valley, along the Shebelle River in Ogaden (Somali Region), and in the western part of the country on the border with South Sudan.

CLINICAL FEATURES

- **Acute presentation**
    - **Swimmer's itch**: Itchy rash ("swimmer's itch") after swimming. Pruritic papular or urticarial rash.
    - **Acute schistosomiasis syndrome (Katayama fever):** fever, chills, myalgia, arthralgia, dry cough, diarrhea, abdominal pain, diarrhea urticaria and angioedema
- **Intestinal schistosomiasis**
    - Chronic or intermittent abdominal pain, poor appetite, and diarrhea.
    - Chronic colonic ulceration: intestinal bleeding, iron deficiency anemia
    - Bowel strictures: obstruction or acute abdomen with inflammatory mass
- **Hepatosplenic schistosomiasis**: splenomegaly, distended abdominal wall vessels
- **Pulmonary complication (in those hepatosplenic schistosomiasis)**
    - Dyspnea; Eggs being embolized in to the pulmonary circulation, resulting in pulmonary hypertension, military pulmonary infiltrates
- **Glomerular disease**: Immune complex glomerulonephritis
    - Nephritic or nephrotic syndrome presentation

- **Neurologic manifestation**
    - Rapidly progressive transverse myelitis: paraparesis, bowel and bladder dysfunction
    - Brain involvement is possible: focal neurologic deficit, encephalitis
- **Genitourinary schistosomiasis**
    - Terminal hematuria, in severe cases total hematuria
    - Dysuria, urinary frequency, urgency
    - Hypertrophic or ulcerative lesions of the genitalia (both men and women)

INVESTIGATIONS

- Stool microscopy for eggs with typical spine: yield is low acute and light infection
- Urine microscopy for eggs with typical spine
- CBC: eosinophilia in acute presentation
- Serologic test (antibody test): a negative antibody test is can exclude infection
- Biopsy specimens: egg and granulomatous inflammation
- Imaging: Ultrasound for hepatosplenic schistosomiasis, cystoscopy/IVU for genitourinary, MRI for neurologic, echocardiography/Chest X-ray for pulmonary manifestation

Treatment

Objectives

- Eradicate the infection
- Reversing acute or early chronic disease
- Prevent complications

Pharmacologic

First line

- **Praziquantel,** 40 mg/kg in one or two divided doses (4-6 hours apart) on one day for both
  - Adverse effects: abdominal cramp, vomiting, dizziness, headache, vomiting, abdominal pain, diarrhea, and pruritus.
  - Paradoxical hypersensitivity reactions may be observed with acute infection and/or in early chronic schistosomiasis.
- **Acute schistosomiasis syndrome**
  - Prednisolone 20 to 40 mg daily for five days.
  - Avoid praziquantel until acute symptoms subside and start it along with steroid therapy
- **Neuroschistosomiasis**
  - If neuroschistosomiasis is suspected or proven high dose steroid should be started before praziquantel: prednisolone 1-2mg/kg/day for 2weeks, then tailored/tapered to the individual needs for up to six months.
  - Praziqu**antel,** 40 mg/kg single dose, after few days of steroid therapy.
- **Hepatosplenic schistosomiasis**
  - Treatment for portal hypertension.

Prevention

- Public health measures
  - Water sanitation programs:
  - Safe water supplies
  - Minimizing contact with fresh water or wearing protective clothing and footwear

  - Vigorous toweling of exposed skin and/or applying insect repellent DEET (N,N-diethyl-m-toluamide) after exposure to fresh water.
  - Eradication of snails using molluscicides or environmental control of snail breeding sites.
- Mass drug administration (MDA)
  - Praziquantel (non-pregnant and pregnant adults, and children ≥4 years: 40 mg/kg orally once; children <4 years - contraindicated).
  - Annually repeated MDA is appropriate.

FURTHER READING

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2. D J Gray, A G Ross, Yue-Sheng et al. Diagnosis and management of schistosomiasis. *BMJ* 2011;342: d2651

8.23 FILARIASIS, LYMPHATIC (ELEPHANTIASIS)

BRIEF DESCRIPTION

- The term filariasis refers generally to disease caused by the lymphatic-dwelling filarial worms *Wucheria bancrofti, Brugia malayi, and Brugia timori.*
- *Wuchereria bancrofti* is the most common cause of lymphatic filariasis in the Tropics including Ethiopia.
- The infection is transmitted by mosquitoes. Filarial parasites exhibit a daily periodicity in the concentration of microfilariae in the peripheral blood.
- The main clinical presentation (lymphedema) is also the main feature of podoconiosis (“non-filarial elephantiasis”). Podoconiosis is a non- infectious disease is a geochemical disease occurring in individuals exposed to red clay soil of volcanic origin.

- Lymphatic filariasis is found in several districts of SNNP, Oromiya, Amhara, Benishangul Gumuz, and Gambella.
- Podoconiosis is also widespread in six regional states in the country (Amhara, Benishangul Gumuz, Oromia, SNNPR, Somali and Tigray)

CLINICAL FEATURES

- **Progressive filariasis:** In progressive filariasis, the clinical features depend on the clinical stage.
    - Asymptomatic amicrofilariaemic stage: No clinical symptom
    - Asymptomatic microfilariaemic stage: No clinical symptoms but microfilariae detectable
    - Stage of acute manifestations:
        - Filarial fever (ADL-DLA)
        - Acute adenolymphangitis (ADL): high fever, lymphatic enlargement, local edema, tenderness and redness of overlying skin. Ulceration can occur.
        - Dermatolymphangioadenitis (DLA): high fever, chills, muscle aches, and headache with inflammatory skin changes in the area of infection.
    - Lymphangitis
    - Lymphadenitis
    - Epididimorchitis
- Stage of obstructive (chronic) lesions: 5-15 years
    - Leg lymphedemas or hydrocele (see the table below for staging of lymphedema)
    - Chyluria: milky urine. Lymph being intermittently discharged in the urine. This can lead to malnutrition

Table 8.59: Stages of lymphedema in chronic lymphatic filariasis

	Swelling	Skin folds	Apearance
Stage I	Reversible at night	Absent	Smooth, normal
Stage II	Not reversible at night	Absent	Smooth, normal
Stage III	Not reversible at night	Shallow	Smooth, normal
Stage IV	Not reversible at night	Shallow	Irregular, occasional knobs or nodules
Stage V	Not reversible at night	Deep	Smooth or irregular
Stage VI	Not reversible at night	Shallow or deep	Wart-like lesions on foot or toes
Stage VII	Not reversible at night	Deep	Irregular; needs help with daily activities; dependent

- Occult or cryptic filariasis, presenting as tropical pulmonary eosinophilic (TPE) syndrome:
  - Occult filariasis results from hyper-responsiveness to filarial antigens.
  - Classic manifestations are: paroxysmal cough and wheeze, scanty sputum, occasional hemoptysis, adenopathy, chronic interstitial lung disease, recurrent low- grade fever, and weight loss.

Investigations and diagnosis

- Lymphatic filariasis should be suspected in individuals living in districts known to have the disease who present with typical acute manifestations (see above) or chronic manifestations (lymphedema, chyluria, hydrocele).
- Definitive diagnosis is established by either of the following
  - Blood film:

      - Demonstration of microfilariae in peripheral blood film (Giemsa or wright stain):
      - Due to the nocturnal periodicity; the greatest number of microfilariae can be found in blood between 10:00 PM and 2:00 AM.
  - Detection of circulating filarial antigen
- CBC: extremely high eosinophil count.
- Imaging
  - Ultrasonography: adult worms may be visualized in the lymphatics of the female breast or male scrotum

TREATMENT

OBJECTIVES

- Eradicate the filaria
- Prevent complications

Non pharmacologic

- Supportive treatment and prevention of acute ADL attacks:
  - Hydration and rest
  - antipyretics and analgesics
  - Treatment and prevention of lymphedema: Hygiene measures for the affected limb:
  - Wash twice daily with soap and clean water and dry well
  - Keep nails short and clean
  - Elevate the affected limb at night
  - Wear comfortable footwear
  - Prevent and treat entry lesions
  - Frequent exercise of the affected limb to promote lymph flow

  - Standing on toes, flexing and circling ankles while sitting
- Use of antibiotic or antifungal agents:
  - antiseptic, antibiotic, and antifungal creams for small wounds and abrasions
  - systemic antibiotics or antifungals in severe cases
- Surgical treatment of hydrocele

Pharmacologic

- Recommended regimen for lymphatic filariasis in clinical settings:
  - **Diethylcarbamazine citrate (DEC)**, 6mg/kg P.O. daily for 12 days

    OR
  - **Diethylcarbamazine citrate**, 6 mg/kgp. P.O. PLUS **albendazole** 400mg P.O., as single dose.
  - DEC should not be used in patients with onchocerciasis, due to possible severe adverse reactions (fatal encephalopathy).
  - Patients should be examined for co-infection before using DEC. In co-infected patients, the following alternative regimen should be used:
    - **Ivermectin**, 200-400micrograms/kg P.O., plus **albendazole** 400mg P.O. as single dose
  - **N.B.** Ivermectin should not be used in patients with loiasis.

Table 8.60: Treatment of lymphatic filariasis among adults

Infection status	Clinical condition	Treatment
Lymphatic filariasis (Mono-infection)	lymphatic filariasis with clinical symptoms or not	single-dose DEC (6 mg/kg), ± doxycycline (200 mg/day for 4 to 6 weeks)
	has tropical pulmonary eosinophilia due to W. bancrofti	14 to 21 days of DEC (6 mg/kg/day) ± doxycycline (200 mg/day for 4 to 6 weeks)
Concomitant infection: lymphatic filariasis with Onchocerciasis	without ocular involvement	DEC is contraindicated with Onchocerciasis; Thus, first ivermectin (150 mcg/kg single dose) followed by DEC treatment as above (***after 1 month of ivrmectin***)
	with ocular involvement	doxycycline 200 mg orally once daily for 4 to 6 weeks) followed by ivermectin 150 mcg/kg orally single dose
Concomitant infection: lymphatic filariasis with Loiasis	<2500 Loa loa microfilariae/mL of blood	DEC standard regimen for loiasis (8 to 10 mg/kg/day for 21 days)
	2500 to 8000 L.loa microfilariae/mL of blood	ivermectin pretreatment, followed by DEC
	> 8000 L.loa microfilariae/mL of blood	doxycycline (200 mg/day once orally for 4 to 6 weeks) or Albendazole (200 to 400 mg BID for 21 days, with fatty meal)

PREVENTION

- Mass drug administration (MDA)
  - Annual single dose of DEC 6mg/kg PLUS Albendazole 400 mg, yearly for 4-6 years in areas where onchocerciasis is not co-endemic with filariasis.

  - In areas where onchocerciasis is present but loiasis is absent: Annual single dose of Ivermectin 200-400 micrograms/kg PLUS Albendazole 400 mg, yearly for 4-6years.
- Vector control

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1. Belete Mengistu, Kebede Deribe, Fikreab Kebede et al. The National Programme to Eliminate Lymphatic Filariasis from Ethiopia. Ethiop Med J. 2017; 55(Suppl 1): 45–54.

8.24 ONCHOCERCIASIS

BRIEF DESCRIPTION

- Onchocerciasis is a disease caused by *Onchocerca volvulus*, transmitted by several species of simulium ("Black flies") and manifested by onchodermatitis.
- Humans are the only definitive host for O. volvulus. Thy are infected via the bite of a blackfly of the Simulium genus.
- The blackfly deposits infective third-stage larvae into the human skin, which mature into adult parasites (macrofilariae) over 6-12 months
- The adult worms (macrofilariae) become encapsulated by fibrous tissue and form subcutaneous nodules, often overlying bony prominences. They move through subcutaneous, dermal, and ocular tissues and the lymph system.
- The microfilariae induce minimal immune response while alive but when

they die, they induce a much more intense inflammatory response.

- Onchocerciasis is endemic in SNNPR, Amhara, Beneshangul-Gumuz and Oromia regions taking the total to over 16.3 million people being at risk.

CLINICAL FEATURES

- **Onchocercal dermatitis**
    - Acute papular onchodermatitis: small pruritic papules, vesicles, or pustules
    - Chronic papular onchodermatitis: Large, flat-topped, pruritic papules, symmetrically distributed over buttocks, waist, and shoulders.
    - Lichenified onchodermatitis: hyperpigmented pruritic papules and plaques limited to one limb.
    - Hanging groin: inguinal lymph nodes enlarge over atrophic thigh skin. When the nodes shrink and they leave redundant folds skin.
    - Skin atrophy
    - Depigmentation: Depigmentation (leopard skin) typically occurs on the anterior shins of older adults
- **Oncocercoma**
    - Subcutaneous nodules that contain adult worms may be visible or palpable.
    - Typically appear over bony prominences
- **Oncular onchocerciasis**
    - Punctate keratitis
    - Sclerosing keratitis
    - Uveitis, chorioretinitis
    - Optic atrophy
    - Eventually blindness

INVESTIGATION AND DIAGNOSIS

- **Skin snips: for demonstration of motile microfilaria**
    - The gold standard for diagnosis.
    - At least two bloodless skin snip taken with a small needle or disposable razor blade (the pelvic girdle, buttocks, and external thigh are preferred sites)
    - The sample is incubated in saline for 24 hours before examination.
- **Slit-lamp examination**:
    - Slit-lamp examination can be used to look for motile microfilariae within the anterior chamber of the eye.
    - Prior the examination sitting forward (with the head between the knees) for at least 2 minutes
- **Ultrasonography**: Ultrasound of the subcutaneous nodules to look form identification of adult worms.

TREATMENT

OBJECTIVE

- Relieve itching
- Treat the infection

Non pharmacologic

- Surgical removal of accessible onchocercomas (Nodulectomy has a place for eradication of the adult worm)
- Minimize fly bites by avoiding fly-infested areas, wearing protective clothing and using insect repellents

Pharmacologic

- **Ivermectin is the first line**

Table 8.61: Treatment of individuals with onchocerciasis

Level of transmission	Regimen
Patients in endemic areas (with high levels of ongoing transmission)	**Ivermectin** 150 mcg/kg orally (single dose, on empty stomach with water); repeat every three to six months or once per year until asymptomatic; Dosage forms: Tablet, 3mg, 6mg (scored)
Patients outside endemic areas or in areas with low transmission	**Ivermectin** 150 mcg/kg orally (single dose) PLUS **Doxycycline** 200 mg orally once daily for six weeks (start one week after administration of ivermectin)

- **Adverse reactions during ivermectin administration**
    - Generally mild reactions occur as a result of the host immune response to released antigens.
    - Symptoms usually develop within three days of treatment: fever, skin rash or itching, dizziness, myalgia, arthralgia, headache, and tender lymphadenopathy.
    - Severe reactions e.g., hypotension can also occasionally occur.
    - Symptoms can usually be managed with analgesics and antihistamines.

E.g., Promethazine, 25mg BID OR TID until the pruritis subsides.

- **Prevention**
    - Mass drug administration programs
        - Ivermectin at 6 to 12 monthly intervals for 10 to 16 years.
        - In areas where both onchocerciasis and loiasis may be endemic, assessment for loiasis should be made prior to mass treatment with ivermectin.

- **Loa loa coinfection**
  - Before any onchocerciasis treatment began, make sure that no Loa loa co-infection, another filarial parasite.
  - Ivermectin can facilitate entry of L. loa microfilariae into the central nervous system, leading to encephalopathy.
    - The optimal treatment of onchocerciasis and loiasis coinfection is uncertain: Doxycycline (200 mg orally once daily for six weeks) plus Albendazole (400 mg orally with fatty meal twice daily for three weeks).

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8.25 RABIES

BRIEF DESCRIPTION

- Rabies is a fatal viral disease that can affect almost all mammals.
- The causative agent is Rabies virus from class Rhabdoviridae, genus *Lyssavirus* and species Serotype 1.
- The virus is transmitted through inoculation of saliva, usually from the bite of an infected animal.
- More than 95% of the deaths are due to exposure to dogs, which are the major reservoir and transmitter of rabies, but transmission by wild

animals such as bats, foxes, and wolves is also possible.

- The incubation period is relatively long (3 weeks to 3 months) but can be as long as several years in rare cases. The closer the inoculation site is to the central nervous system, the shorter the incubation period.

CLINICAL FEATURES

- **Prodrome** (2-10 days):
  - Paresthesia (pins and needles sensation) around bite: very suggestive of rabies.
  - Fever, headache, malaise, muscle pain, nausea, vomiting, and cough.
- **Encephalitic rabies: Acute neurologic phase** (2-7 days):
  - Confusion, delirium, altered mentation, agitation, hallucinations.
  - Spasms in response to touch, noise, visual, or olfactory stimuli.
  - Phobic spasms: hydrophobia (fear of water) and aerophobia (fear of air): strong evidence for rabies.
  - Autonomic system dysfunction: enlarged pupils, increased production of saliva, tears, perspiration
  - Generalized arousal or hyperexcitability associated with disorientation, fluctuating consciousness, restlessness, agitation, and visual or auditory hallucinations.
  - Coma, death (0-14days)
    - Occurs after several days to 1 week.
    - Hypoventilation, loss of temperature control, heart dysfunction can lead to death.
- **Paralytic rabies (Ascending paralysis)**
  - Similar to Guillain-Barré syndrome, occurs in some cases and makes diagnosis more difficult. This can also occur during post-exposure rabies treatment.

INVESTIGATIONS AND DIAGNOSIS

- Diagnosis rests on history of exposure and typical neurological findings.
- CSF: increased white cells (lymphocytes), mildly increased protein.
- Laboratory confirmation is usually postmortem

TREATMENT

- There is no effective treatment against rabies.
- It is almost always fatal.
- Supportive management is important. Recovery is exceedingly rare and has only occurred in cases where intensive respiratory and cardiac supports were available.
- Apparently healthy dogs and cats at the origin of the exposure should be kept under observation for 10 days.
- Dogs and cats that are suspected of being rabid, as well as wild animals, should be humanely killed and their tissues examined in the appropriate laboratory.

Objectives

- Reduce the pain and suffering of patient.

Non pharmacologic

- Supportive treatment of a paralyzed patient mostly focused on nursing care and providing comfort to the patient.

Pharmacologic

Palliative care

- The short clinical course of rabies entails much suffering.
- Patients remain conscious, are often aware of the nature of their illness and very agitated.
- Provide adequate sedation and comfort with emotional and physical support.

- IV morphine: relieve severe agitation and phobic spasms. Sedation with barbiturates can be added.
- Avoid intubation and other life support measures when the diagnosis is certain.

HEALTH WORKER SAFETY

- It is theoretically possible for person-to-person rabies though this has not been described.
- As a precaution staff must wear mask, gloves, and goggles.
- Post-exposure prophylaxis is required if a percutaneous, mucous membrane, or non-intact skin exposure to patient's body fluids or tissue occurred.

RABIES POST EXPOSURE PROPHYLAXIS (PEP)

RABIES POST-EXPOSURE VACCINATION AFTER ANIMAL BITES

- **Wound care**
  - The cornerstone of rabies prevention is wound care: potentially reduces the risk of rabies by 90%.
    - Immediately scrub with soap and water, and flush with water for 15 minutes
    - Irrigate with Povidone-iodine
- **Vaccination**
  - Decide on post-exposure vaccination and immunoglobulin use depending on the type of contact with the rabid animal.

Table 8.62: Postexposure prophylaxis (PEP)

Category of exposure	Description	Post-exposure prophylaxes
Category I	Touching or feeding animals, licks on the skin, contact of intact skin with secretions or excretions of rabid animal or person.	No PEP is required Wash exposed skin Surfaces.
Category II	Nibbling of uncovered skin, minor scratches or abrasions without bleeding	Wound washing and immediate vaccination
Category III	Single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches	Wound washing and Immediate vaccination and administration of rabies immunoglobulin

- **Vaccination:**
  - IM doses of 1ml or 0.5ml given as 4 - 5 doses over 4 weeks.
  - One dose of the vaccine should be administered on days 0, 3, 7, 14, and 30.
  - Abbreviated multisite schedule: 2-1-1 regimen: 1 dose is given in the right arm, 1 dose in the left arm at day 0, and 1 dose applied in the deltoid muscle on days 7 & 21
  - All intramuscular injections must be given into the deltoid region.
  - The vaccine should never be administered in the gluteal region.
- **If prior pre-or post-exposure vaccination:**

  - 2 IM doses separated by 3 days are sufficient.
  - Rabies immunoglobulin treatment is not indicated in such cases.
- **Intradermal vaccination:** smaller doses of cell-derived vaccines are also used. The schedules are different than IM schedules.
- **Immunoglobulin:**
  - **Human rabies immune globulin** 20 IU/kg

    OR

  - **Equine rabies immunoglobulin** 40 IU/kg
- **Pre-exposure vaccination**
  - Pre-exposure vaccination is recommended for those in rabies diagnostic and research laboratories and veterinarians, individuals at high risk of exposure such as stray dog handlers, park officials, or bat handlers.
  - Pre-exposure vaccination is administered as 1 full dose vaccine given 3 times, IM or 0.1 ml intradermal, on days 0, 7, and 21 or 28.

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8.26 TETANUS

BRIEF DESCRIPTION

- Tetanus is a vaccine-preventable disease that is caused by a potent neurotoxin produced by the spore-forming bacterium *Clostridium tetani*.
- The spores of *C. tetani* are present in the environment and can contaminate wounds, minor abrasions, and, in neonatal tetanus, the umbilical stump.
- In anaerobic conditions, the spores of *C. tetani* produce vegetative bacteria, which express the tetanus toxin and cause the disease.
- Tetanus toxin is highly neutrotoxic. It inhibits inhibitory neurotransmission. This loss of inhibition (disinhibition) results in increased muscle tone, painful spasms, and widespread autonomic instability.
- In the majority of cases, tetanus arises from minor skin cuts or abrasions. In significant number of patients, no obvious entry site is seen.
- Tetanus can present in one of four clinical patterns:
    - Generalized
    - Local
    - Cephalic
    - Neonatal
- The incubation period = the time from presumed infection (injury) to the first symptom.
- The period of onset = the time between the first symptom and first spasm.
- Incubation period of less than 7 days and a period of onset of 48 hr considered to indicate poor prognosis. However, the time from first symptom to hospitalization and the presence of spasms at presentation have greater prognostic significance
- Prognosis also depends on the severity.

CLINICAL FEATURES

- **Generalized tetanus**
    - Trismus (lockjaw)
    - Spasms: very painful spasms
        - Triggered by noises or other sensory, contact or light.
        - Stiff neck, opisthotonus, risus sardonicus (ironic smile), a board-like rigid abdomen.
        - Periods of apnea or upper airway obstruction
        - Dysphagia
    - Autonomic over activity: restlessness, profuse sweating, and tachycardia, cardiac arrhythmias, labile hypertension or hypotension, and fever are often present.
- **Local** tetanus: Rarely, tetanus presents with tonic and spastic muscle contractions in one extremity or body region.
- Cephalic tetanus: Patients with injuries to the head or neck may present with cephalic tetanus, involving initially only cranial nerves.
- Investigations and diagnosis
- The diagnosis of tetanus is clinical based on the typical findings
- Severity Scoring: There is several severity scores used but the Ablett classification has been used most commonly.

Table 8.63: Ablett classification of severity of Tetanus

Grading	Clinical features
I- Mild	Mild to moderate trismus; general spasticity; no respiratory embarrassment; no spasm; little or no dysphagia
II- Moderate	Moderate trismus; well-marked rigidity; mild to moderate but short spasms; moderate respiratory embarrasement with RR greater than 30; mild dysphagia

III-Severe	Severe trismus; generalized spasticity; reflex prolonged spasms; increased RR greater than 40; apnoeic spells; severe dysphagia; tachycardia greater than 120.
IV-Very Severe	Grade III and violent autonomic disturbances involving the cardiovascular system. Severe hypertension and tachycardia alternating with relative hypotension and bradycardia, either of which may be persistent.
Ablett JJL. Ellis M, ed. Symposium on Tetanus in Great Britain. 1967;1-10.	

TREATMENT

OBJECTIVES

- Airway management and other general supportive management
- Control of muscle spasms and prevent serious complications like laryngeal spasm
- Halting the toxin production and neutralization of the unbound toxin
- Management of dysautonomia

SUPPORTIVE TREATMENT

- Admit patients to a quiet, low-light(darker), and in severe cases, to an intensive care unit, if possible, for continuous cardio-pulmonary monitoring.
- In severe tetanus, early tracheostomy and mechanical ventilation are needed.
    - In mechanically ventilated patients, higher doses of diazepam. Neuromuscular blockage can also be safely employed.
- Bed sore prevention, thromboembolism prophylaxis, stress ulcer prophylaxis is needed.
- Avoid stimuli.
- Nutritional support and hydration measures are important.

PHARMACOLOGIC

- Patients with severe tetanus should be managed in the intensive care setting where mechanical ventilator and appropriate medication are available.
- This may necessitate referral of most patients to specialized centers.

CONTROL OF SPASMS

- **Diazepam**, 10 mg I.V. should be given every 4 hourly, the dose being titrated depending on the response.
    - Large doses (as high as 250mg in 24 hour) can be used, in mechanically ventilated patients only.As large doses can cause respiratory depression.

PLUS

- **Chlorpromazine**, 25-50mg IM alternating with diazepam.

PLUS

- **Magnesium sulphate**, loading dose of 40mg/kg IV over 30 min, followed by IV infusion of 2g/h for patients over 45kg and 1.5g/h for patients 45kg or under. It is used in patients with severe tetanus for whom tracheostomy has been done)

NEUROMUSCULAR BLOCKADE

- Neuromuscular blocking agents are used when sedation alone is inadequate.
    - **Suxamethonium,** 20-100mg I.V. depending on the effect with mechanical ventilation may be employed in patients with severe laryngeal spasm.

HALTING TOXIN PRODUCTION AND NEUTRALIZING CIRCULATING TOXINS

- Wound debridement, removing necrotic tissue and foreign bodies
- Antimicrobial treatment
    - **Metronidazole**, 500mg I.V, TID for 7-10 days
    - Neutralization of circulating (unbound) toxin.
    - **Tetanus antitoxin (TAT)** 10,000 IU IM after a skin test (a skin test done **by** 0.1 ml in a 1:10 dilution)

- If available: Human Tetanus immunoglobulin (HTG) 500IU, IM stat (preferred over TAT)

CONTROL OF AUTONOMIC DYSFUNCTION

- **Magnesium sulphate** (see above)

PLUS

- **Labetalol** : 0.25 to 1.0 mg/min infusion
  - Beta blockade alone, like propranolol, should be avoided because of reports of sudden death.

PLUS

- **Morphine** sulfate (0.5 to 1.0 mg/kg per hour by continuous intravenous infusion) can be added.

Drug name	**dose**	**Comment**
Control of spasm		
Diazepam	10 mg I.V. should be given every 4 hourly, the dose being titrated depending on the response.	Be cautious with respiratory depression at high dose, if not mechanically ventilated.
Neuromuscular blockade		
Suxamethonium	20-100mg I.V.	May be employed in patients with severe laryngeal spasm.
Control of autonomic dysfunction		
Magnesium sulphate	Load 40mg/kg IV over 30 min, then IV infusion of 2g/h for > 45kg & 1.5g/h for ≤45kg	well-studied in reducing autonomic instabilities; help to reduce spasms

Labetolol	0.25-1.0mg/min IV infusion	Alpha and beta blocker, avoid beta blockers alone
Morphine	0.5-1.0mg/kg per hour	
Halting toxin production and neutralizing circulating toxins		
Wound debridement to eradicate spores and necrotic tissue	Initially and as necessary	Halt bacteria germination and related toxin production
Human Tetanus immunoglobulin (HTG)	500 IU I.M. single dose	Start immediately. Help to neutralize unbound circulating toxins
Tetanus Antitoxin (TAT)	10,000 IU IM.	Start immediately. after a skin test or history taking

PREVENTION

- Immunization
- Post exposure
    - Clean wound and minor wounds; Vaccination alone
    - All other wounds:
    - Human tetanus immunoglobulin IM 250 IU. Because it is not available, TAT is used: **TAT: 1,500 IU IM**

      PLUS
    - Vaccination (TT) for previously not fully vaccinated or vaccinated before 5-10 years).
    - Immunization of pregnant or childbearing age women reduces neonatal tetanus mortality by more than 90 %.

- Improving hygiene during home births is also help to prevent neonatal tetanus.

FURTHER READING

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8.27 TUBERCULOSIS

8.27.1 DRUG SUSCEPTIBLE TUBERCULOSIS

BRIEF DESCRIPTION

- Tuberculosisis is a chronic bacterial infection caused by a group of bacteria, *Mycobacterium tuberculosis complex,* the most common of which is Mycobacterium tuberculosis. Less frequently, it can be caused by *Mycobacterium bovis* and *Mycobacterium africanum.*
- Tuberculosis usually affects the lungs in which case it is called pulmonary TB.
- In addition to the lungs, any part of the body can be affected with this bacterium and in this case, it is called extra-pulmonary TB.
- Common extra-pulmonary sites affected include the lymph nodes, pleura, spine, urinary tract, the brain, joints, bone and abdomen.
- HIV infection is one of the most important risk factors for the development of active tuberculosis.

CLINICAL FEATURES

- The clinical features of tuberculosis depend on the specific organ affected.
- The clinical features can be grouped: general (non-specific) and organ specific

- The general symptoms of TB (pulmonary or extra-pulmonary):
  - Weight loss, fever, night sweats, loss of appetite, fatigue, malaise
  - Malnourished and chronically sick appearance
- Organ specific
  - Pulmonary tuberculosis
    - Cough that lasts for more than 2 weeks with or without sputum production
    - Chest pain
    - Hemoptysis
    - Shortness of breath
  - Tuberculous lymphadenitis
    - Slowly growing painless lymph node enlargement
    - Initially firm and discrete, later become matted and fluctuant.
    - Formation of abscesses and discharging sinuses, which heal with scarring.
  - Tuberculous pleurisy
    - Pleuritic chest pain (pain while breathing/coughing/sneezing)
    - Intermittent cough
    - Shortness of breath
    - Signs of pleural effusion (dullness, decreased/absent air entry and decreased tactile fremitus)
  - TB of bones and/or joints
    - Localized pain and/or swelling +/- discharge, stiffness of joints
    - Spine (TB spondylitis): localized swelling over the back(gibbus), back pain paralysis (weakness of the lower extremities)

- Abdominal TB
    - Chronic non-specific abdominal pain with diarrhea or constipation,
    - Fluid in the abdominal cavity (ascites).
    - Mass (inflammatory mass) in the abdomen
- Tuberculous meningitis
    - Headache, fever, vomiting: insidious onset
    - Neck stiffness, impaired level of consciousness.
- Tuberculous pericarditis
    - Chest pain (pleuritic)
    - Shortness of breath
    - Pericardial friction rub or distant heart sounds

INVESTIGATIONS AND DIAGNOSIS

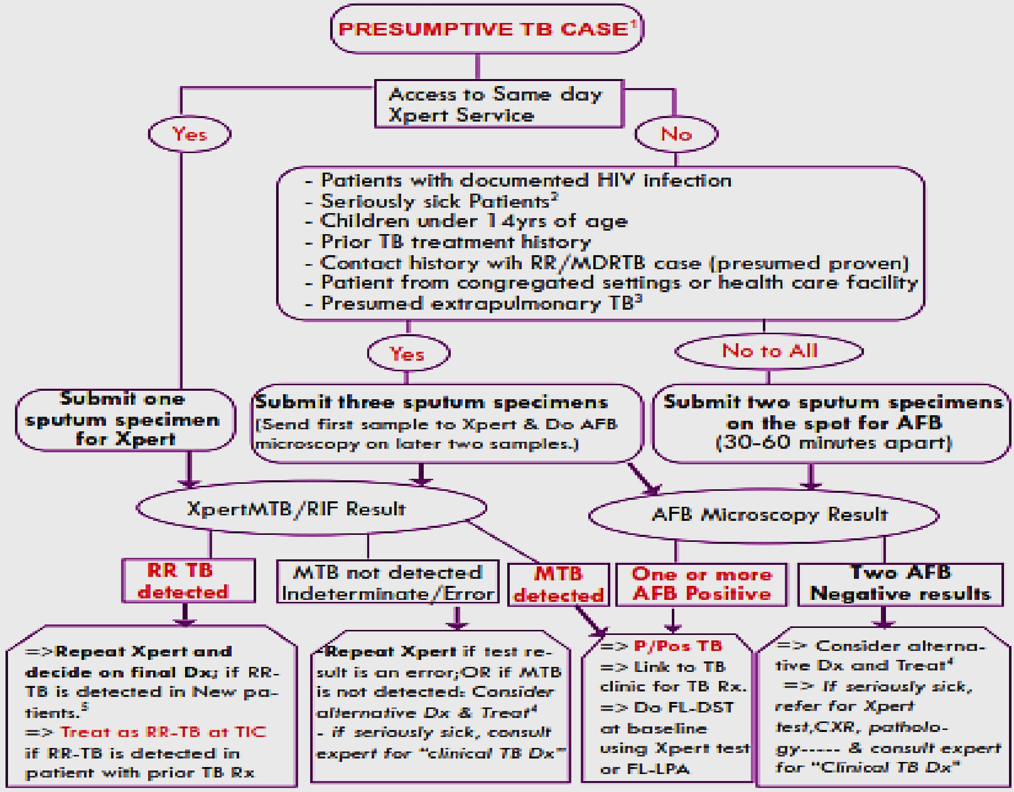
- The diagnosis of tuberculosis requires clinical suspicion and microbiologic identification of the bacilli.
- Microbiologic tests to identify the bacilli
    - **Sputum direct microscopy**: Ziehl Nielsen (acid fast bacilli) (**AFB**) staining
        - Three sputum specimens (SPOT-EARLY MORNING-SPOT) need to be collected and examined in two consecutive days
        - Result must be available on the second day.
    - **Gene Xpert MTB/RIF**
        - A fully automated DNA/molecular diagnostic test to detect TB and Rifampicin resistance simultaneously.
        - It is recommended as the initial diagnostic test for all persons being evaluated for TB.

  - **Sputum culture and drug susceptibility**
    - Culture is the gold standard
    - It takes weeks to get the results.
    - If sputum AFB and/or Gene Xpert are negative and there is a strong suspicion, sputum culture can be sent to a referral laboratory. However, treatment for an alternative diagnosis or “clinical TB” should not be delayed.
  - **Line Probe Assay (LPA)**
    - A test to identify the presence of specific mutations on the genes of TB bacilli which are responsible for Isoniazid and Rifampicin resistance.
    - It is a rapid and accurate test to identify cases with MDR-TB.
    - The test may be available in referral laboratory for patients suspected of MDR-TB.
- Body fluid analysis and identification of pathogen
  - Pleural fluid, ascitic fluid, CSF
    - Cell count with differential
    - Protein, glucose
    - LDH
    - Gene Xpert
    - Cytology (cytopathology)
- Fine needle aspiration and histopathologic examination: enlarged lymph nodes
- Tissue biopsy and histopathology: pleural, skin, endometrium, bronchial, colon/cecum, liver
- Imaging:

- Chest X-ray.
- Depending on the suspected extra pulmonary sites other imaging modalities may be needed: abdominal ultrasound, brain/spinal MRI, Joint/bone X-ray, image guided FNA or biopsy

- Other investigation: HIV test, CBC, ESR, CSF analysis

Figure 1: National Diagnostic Algorithm for Patients with Presumptive TB


PRESUMPTIVE TB CASE1
Access to Same day Xpert Service
Yes
No
- Patients with documented HIV infection
- Seriously sick Patients2
- Children under 14yrs of age
- Prior TB treatment history
- Contact history wih RR/MDRTB case (presumed proven)
- Patient from congregated settings or health care facility
- Presumed extrapulmonary TB3
Yes
No to All
Submit one sputum specimen for Xpert
Submit three sputum specimens (Send first sample to Xpert & Do AFB microscopy on later two samples.)
Submit two sputum specimens on the spot for AFB (30-60 minutes apart)
XpertMTB/RIF Result
AFB Microscopy Result
RR TB detected
MTB not detected Indeterminate/Error
MTB detected
One or more AFB Positive
Two AFB Negative results
=>Repeat Xpert and decide on final Dx; if RR-TB is detected in New patients.5
=> Treat as RR-TB at TIC if RR-TB is detected in patient with prior TB Rx
Repeat Xpert if test result is an error;OR if MTB is not detected: Consider alternative Dx & Treat4
- if seriously sick, consult expert for "clinical TB Dx"
=> P/Pos TB
=> Link to TB clinic for TB Rx.
=> Do FL-DST at baseline using Xpert test or FL-LPA
=> Consider alternative Dx and Treat4
=> If seriously sick, refer for Xpert test,CXR, pathology----- & consult expert for "Clinical TB Dx"

[1] Presumptive TB is defined by symptoms & signs consistent with TB; mainly Persistent cough of two or more weeks(or cough of any duration if HIV positives).

[2] In seriously sick patients for whom "HIV test is not done", Available investigations including xpert, CXR and HIV testing may be done in one –go to avoid delays and save patients 'live.Such patient are advised to be managed at Hospital level.

[3] liquid Specimens from EPTB site(e.g. CSF)may be subjected to xpert test without additional processing.

[4] Broad spectrum antimicrobials,excluding fluoroquinolone or anti-TB drugs is to be given for 10-14days.

[5] one RR-TB xpert result in population groups with low DR-TB risk(<5%)needs to be **repeated** on fresh specimen.if repeat test detects RR-TB,link to TIC for Second line Anti-TB; if repeat test only detects MTB but not RR-TB,initiate first line Anti-TB treatment and monitor response.

Case definitions

- **A case of tuberculosis**: is a definite case of TB or a patient whom an experienced health worker has diagnosed TB and has decided to treat the patient with a full course of TB treatment.
- **A definite/proven case of tuberculosis** is a patient with either of the following
    - Two sputum smears (one sputum positive is enough for HIV positive patients)

      OR
    - Sputum culture positive for Mycobacterium tuberculosis.

      OR
    - Mycobacterium tuberculosis is identified from a clinical specimen, either by culture or by a newer molecular technique.

TREATMENT OF DRUG SUSCEPTIBLE TB

Objectives

- Cure
- Prevent death from active TB or its late complications
- Restore quality of life and productivity
- Decrease transmission
- Prevent relapse
- Prevent the development and transmission of medicine resistance

Non pharmacologic

- Counseling: adherence, the nature of treatment, contact screening
- Good nutrition
- Adequate rest

- Admission for severely ill patients e.g., Tb meningitis, pericarditis

Pharmacologic

- Standardized combination treatment: all patients in a defined group receive the same treatment regimen.
- A combination of 4 or more anti-TB medicines.
- Directly observed treatment (DOT)

First line anti-TB Medicines

- The first line anti-TB medicines available for TB treatment in Ethiopia are:
    - **Rifampicin (R):** the most bactericidal and potent sterilizing agent
    - **Isoniazid (H):** highly bactericidal especially in the first few days
    - **Pyrazinamide (Z):** only active in acidic environment and bacilli inside macrophages
    - **Ethambutol (E):** bacteriostatic and effective to prevent drug resistance when administered with other potent drugs

Table 8.64: The essential anti-TB drugs and their dose recommendations

Recommended adult dose and children ≥ 25 kg body weight		First line TB drugs	Recommended pediatric dose	
Daily dose (mg/kg weight)	Maximum (mg)		Daily dose (mg/kg weight)	Maximum (mg)
5 (4-6)	300	**Isoniazid (H)**	10 (7–15)	300
10 (8-12)	600	**Rifampicin (R)**	15 (10–20)	600
25 (20-30)	2,000	**Pyrazinamide (Z)**	35 (30–40)	-
15 (15-20)	1,600	**Ethambutol (E)**	20 (15–25)	-

- **Standardized first line treatment regimen for new drug susceptible (presumed to be drug susceptible) tuberculosis**
    - New pulmonary TB (PTB) patients presumed or known to have drug-susceptible TB
    - New extrapulmonary TB (EPTB) patients
        - Standardized regimen: 6 months total (2 months intensive and 4 months continuation phase) 2RHZE/4RH
        - Intensive phase: 2 months Rifampicin, Isoniazid, Pyrazinamide & Ethambutol (2RHZE)
        - Continuation: 4 months Rifampicin and Isoniazid (4RH)

Table 8.65: First line TB treatment adult and pediatric dosing chart using body weight bands

Adult and pediatric ≥25 kg weight			**Pediatrics**			
Patient weight band (kg)	**Regimen and dose in two phases**		**Daily dose (mg/kg weight)**	**Regimen and dose in two phases**		
	Intensive: 2(RHZE)	Continuation: 4(RH)		Intensive:2(RHZE)		Continuation: 4(RH)
				RHZ75/50/150	**E 100**	**RH75/50**
20-29	1 ½	1 ½	4-7kg	1	1	1
30-39	2	2	8-11kg	2	2	2
40-54	3	3	12-15kg	3	3	3
≥55	4	4	16-24kg	4	4	4

- **Previously treated TB patients presumed or known to have drug-susceptible TB**
    - In all previously treated TB patients who require re-treatment, specimen for rapid molecular-based drug susceptibility testing for first line TB

drugs should be obtained at or before the start of treatment.

  - While awaiting the result, the standard first line treatment regimen is recommended: 2(RHZE)/4(RH)
  - A "retreatment regimen" with addition of streptomycin **is not recommended**.

- **Patients who presented with is for patients active TB after known contact with a patient documented to have drug-resistant TB**
  - Sample should be sent for rapid Drug Susceptibility Test (DST)
  - Treatment should be decided based on rapid DST result.
  - While awaiting DST result, the patient may be initiated treatment with the regimen based on the DST of the presumed source case.
- **Extended continuation phase**
  - The following extrapulmonary forms of Tb require prolonged continuation phase
    - CNS (TB meningitis or Tuberculoma)
    - Bone or joint TB (Vertebral (TB spondylitis), joint and osteomyelitis), which require prolongation of the continuation phase for
  - Regimen (a total of 12 months: 2months intensive phase and 10 months continuation phase); 2RHZE/10RH
- **Adjuvant corticosteroid therapy**
  - Adjuvant corticosteroid therapy, dexamethasone or prednisolone tapered over 6-8weeks should be used for patients with the following two extrapulmonary forms
    - TB meningitis
    - TB pericarditis

Table 8.66: Prednisone dose for adult TB patients with TB pericarditis

Weeks of treatment	Prednisolone dosage
1-4	60mg/day
5-8	30mg/day
9-10	15mg/day
11th week	5mg/day (then discontinue at end of 11th week)

- **Corticosteroid for TB meningitis**
  - Dexamethasone 12 mg/day OR Prednisolone 60mg/day for 3 weeks and then decreased gradually during the subsequent 3 weeks.

MONITORING OF PATIENTS ON TREATMENT

- **Clinical monitoring**: during scheduled visit, a patient receiving anti-TB treatment should be checked for the following
  - Persistence or reappearance of clinical feature of TB
  - Weight monitoring: weight is a useful indicator of clinical improvement especially in children and should be monitored monthly.
  - Occurrence of Adverse drug reaction
  - Development of TB complications.
  - Adherence: by reviewing the "treatment supporter card" or UNIT TB register
  - Risk for drug resistance, and need for drug susceptibility testing screening
    - Unsatisfactory response to treatment beyond two months of treatment should alarm the possibility of drug resistance or alternative diagnoses.
- **Bacteriologic monitoring for initially bacteriologically confirmed**

pulmonary TB

- Sputum AFB (direct microscopy) should be done at end of 2nd, 5th and 6th month of therapy.
- Molecular technique like Gene Xpert MTB/RIF cannot be used to monitor treatment as the technique may give false positive result by identifying dead bacilli.
- If AFB positive at the end of second month: send sputum sample for Xpert and line probe assay (LPA) for DST.
  - If at least Rifampicin sensitive: continue to the continuation phase.
  - If Rifampicin resistance: Mark as Rifampicin-resistant Tb (RR-TB) and the outcome is labelled as "MDR TB". Treatment will be started as MDR-TB.
- If AFB is positive at the end of 5th or 6th month: the outcome is treatment failure. DST testing and treatment will proceed as MDR-TB suspect.

- **Management of adverse reaction to First line Anti-TB drugs**
  - Health workers should regularly monitor for occurrence of side effects to the Anti-TB drugs administered to the patient.

Table 8.67: Adverse reactions and drug interactions of first line TB medicines

Medicine	Adverse reaction	Drug interactions
Isoniazid (H)	Skin rash, Sleepiness and lethargy, Peripheral neuropathy (paresthesia, numbness and limb pain), Hepatitis. Rare: Convulsions, pellagra, arthralgia, anemia, lupoid reactions	Al(OH)3 decreases its absorption INH inhibits metabolism of phenytoin, diazepam carbamazepine and warfarin hence increases the serum concentrations

Rifampicin (R)	Gastrointestinal reactions (abdominal pain, nausea, vomiting), Hepatitis, Generalized cutaneous reactions, Thrombocytopenic purpura. Rare: Osteomalacia, pseudomembranous colitis, acute renal failure, shock, hemolytic anemia	Increase metabolism of warfarin, corticosteroids, antifungal agents, protease inhibitors, non- nucleoside reverse transcriptase inhibitors, oral hypoglycemic agents, oral contraceptives hence reduces serum levels of these medicines
Ethambotol (E)	Retrobulbar/Optic neuritis, (impairment of vision, red–green blindness, blurring) Rare: Generalized cutaneous reactions, arthralgia, peripheral neuropathy	
Pyrazinamide (Z)	Arthralgia, Hepatitis; Rare: Gastrointestinal reactions, cutaneous reactions, sideroblastic anaemia	

Table 8.68: Symptom based approach to the management of Anti-TB medicines induced adverse effects

	Adverse-effects	**Responsible Medicines**	**Management**
Minor (Continue Anti-TB medicine/s)	Anorexia, nausea, abdominal pain	Rifampicin; Pyrazinamide	Give tablets with small meals or before bedtime
	Joint pains	Pyrazinamide	NSAIDs
	Burning sensation in feet	Isoniazid	Pyridoxine 100mg daily
	Orange/red urine	Rifampicin	Reassurance

Major (Stop the responsible medicine/s)	Itching, skin reaction	Rifampicin or Isoniazid	Stop and replace with ethambutol; Stop, then reintroduce with desensitization
	Jaundice; hepatitis	Most anti-TB medicines (R, H,Z)	Stop all anti-TB medicines and refer
	Vomiting and confusion	Most anti-TB medicines	Stop all anti-TB medicines and refer
	Visual impairment	Ethambutol	Stop Ethambutol and refer
	Shock, purpura and acute renal failure	Rifampicin	Stop Rifampicin and refer

- **Treatment of patients with renal failure:**
  - In patients with estimated GFR <30ml/min or those on dialysis the dose of Ethambutol and Pyrazinamide need to be reduced from daily to three times per week.
  - Rifampicin and Isoniazid do not need adjustment in patients with renal failure.
  - To reduce Ethambutol and Pyrazinamide without reducing Rifampicin and Isoniazide make using the available fixed drug combinations, use the following regimen.
    - Intensive phase: RHZE three days per week and RH the remaining four days(for 2 months)
    - Continuation phase: RH daily
- **Treatment of patients with (previously known) liver disorder (e.g. hepatitis, cirrhosis):**
  - Most anti-TB medicines can cause liver damage.
  - Do not give Pyrazinamide.

- Isoniazid & Rifampicin plus one or two non- hepatotoxic medicines (Ethambutol and/or Streptomycin) can be used, for a total duration of eight months: 2SERH/6RH
- If the patient has severe liver damage or jaundiced: Streptomycin plus Isoniazid plus Ethambutol in the initial phase followed by Isoniazid & Ethambutol a total duration of 12 months: **2 SHE /10 HE**.

- **Treatment during pregnancy and breast-feeding**
  - Avoid Streptomycin because of the risk of toxic effects on the fetus.
  - Other medicines should not be discontinued during pregnancy or breast-feeding.
  - When a breast-feeding mother has PTB, the infant should, regardless of prior vaccination with BCG, be given chemo-prophylaxis and get BCG vaccination, if not previously vaccinated.
- **Treatment of patients also infected with HIV**
  - All patients with HIV and active TB who are not on ART should be started on ART as described below:
    - CD4 <50 cells/mm3: Initiate ART within 2 weeks of starting TB treatment
    - CD4 counts ≥50 cells/mm: Initiate ART within 8 weeks of starting TB treatment.
    - During pregnancy, regardless of CD4 count: Initiate ART as early as feasible, for to prevent HIV transmission to the infant (AIII).
    - With **tuber**culous meningitis: Initiate ART after 8 weeks of TB treatment.
  - Rifampicin can interact certain ARVS, particularly, some protease inhibitors; hence, drug interaction should be checked.

FURTHER READING

1. National Guidelines of TB, DR-TB and Leprosy in Ethiopia Sixth edition. Federal Ministry of Health Ethiopia, August 2018.

2. TREATMENT OF TUBERCULOSIS Guidelines for treatment of drug-susceptible tuberculosis and patient care. ISBN 978-92-4-155000-0. World Health Organization 2017

8.27.2 DRUG RESISTANT TB

BRIEF DESCRIPTION

- TB is considered drug-resistant (DR) when the causative agent (mycobacterium tuberculosis) is not killed by one or more of the available anti-TB medicines.
- Medicine- resistant TB can be primary or secondary (acquired).
- Primary resistance is medicine resistance among new cases i.e. persons who have never been previously treated for TB.
- Secondary resistance is medicine resistance among previously treated individuals.
- There are five different types of medicine resistance:
  - Mono-resistance: Resistance to one anti-tuberculosis medicine.
  - Poly-resistance: Resistance to more than one anti-tuberculosis medicine, other than Isoniazid and Rifampicin.
  - Multidrug-resistance (MDR)-TB: Resistance to at least isoniazid and rifampicin, two most important first-line drugs.
  - Extensive drug-resistance (XDR-TB): Resistance to any of the fluoroquinolones, and at least one of the injectable Second Line Medicines (capreomycin, kanamycin and Amikacin), in addition to resistance to INH and rifampicin.
    - Since XDR-TB progresses from MDR-TB in two steps, the term “pre–XDR-TB” was introduced to recognize MDR-TB with additional resistance to either one but not both of these classes of medicines.

  - Total drug-resistance (TDR-TB): resistance to all anti TB medicines. The clinical features of medicine susceptible and medicine resistant TB are the same.

INVESTIGATION AND DIAGNOSIS

- Direct smear microscopy
- Gene Xpert MTB/RIF test
- Line Probe Assay (LPA) directly from the sputum specimen or cultured sample
- Culture and Drug Susceptibility Test (DST)
- The definitive diagnosis of medicine-resistant TB depends on laboratory diagnosis through Medicine Susceptibility testing (DST); it requires that M.tuberculosis is isolated and medicine susceptibility test is completed.
- Other investigations: Chest X-ray, HIV test, CBC, urinalysis, FBS, LFT, RFT, Serum electrolyte, TSH, HCG, Audiometric test.

TREATMENT OF MDR-TB

Objectives

- Cure the TB patient and restore quality of life and productivity
- Prevent death from active TB or its late effects
- Prevent TB relapse
- Prevent the development and transmission of extensive medicine resistance
- Decrease transmission

Non pharmacologic

- Surgery (see the adjunct therapies section below)
- Adherence counseling
- Psychosocial and emotional support

- Nutritional support

Pharmacologic

- Treatment **of isoniazid monoresistant TB**
  - Rifampicin, Ethambutol, Pyrazinamide and Levofloxacin for duration of 6 months.
- **Treatment of Rifampicin resistant or Multi drug resistant TB (RR/MDR-TB)**
  - Treatment with second-line TB regimens.
- **Recommended MDR-TB treatment approach**
  - **Standardized treatment approach:** a pre-defined shorter treatment regimen (STR) once the diagnosis of RR-/MDRTB is confirmed using rapid first line DST techniques (i.e., Xpert MTB/RIF or LPA).
  - **Individualized treatment approach:** a regimen tailored to the individual patient when they do not meet the preset criteria to receive the standardized shorter treatment regimen.
  - **Patients who are not eligible for standardized shorter treatment regimen**
    - Confirmed resistance to a medicine in the shorter MDR-TB regimen
    - Exposure to one or more second-line medicines in the shorter MDR-TB regimen for >1 month (unless susceptibility is confirmed)
    - History of Pre-XDR-TB or XDR-TB
    - Intolerance to medicines in the shorter MDR-TB regimen or risk of toxicity
    - Fluoroquinolone resistance
    - Pregnancy

    - Extensive pulmonary TB or severe extrapulmonary TB like CNS TB.
    - Any extrapulmonary disease in people living with HIV
- One or more medicines in the shorter MDR-TB regimen not available**General principles for the use the standardized shorter treatment regimen**
  - ○ Intensive phase: Seven agents administered together for up to 4-6 months
  - ○ Continuation phase (CP): four agents for a fixed duration of 5 months.
  - ○ The "core drugs": Bdq, Mfx, Cfz, and Pto, while Z, E and H are considered as add-on components of the STR.
  - ○ Intensive phase (IP) consists of Bdq, Mfx, Cfz, Z, E, HH, and Pto administered for 4 to 6 months (Bdq better given for 6 months).
  - ○ The continuation phase (CP) consists of Mfx, Cfz, E, and-Z for the fixed duration of 5 months.
  - ○ The regimen: 4 Bdq -Mfx-Pto-Cfz-Z-HH-E / 5 Lfx-Cfz-Z-E
  - ○ Intensive phase may be prolonged up to six months, if the patient remains smear positive after month four of treatment.
- **Individualized DR-TB regimens**
  - ○ For patients for whom the standardized regimens cannot be initiated or cannot be continued with it for clinical reasons or as a result of DST results.
  - ○ It is often needed to be adjusted based on patient clinical history, once additional history or when DST results becomes available.
  - ○ Indications for use of individualized treatment regimens
    - Presumed or confirmed PreXDR-/XDR-TB
    - Known contact with patient failing second line treatment
    - Pregnancy

- Disseminated, meningeal or central nervous system TB
- Any extrapulmonary TB in people living with HIV
- Laboratory evidence of resistance to quinolone or injectable and/or other agents,
- Occurrence of severe drug toxicities,
- Failure of standardized DR-TB treatment
- Re-treatment after treatment interruption beyond eight consecutive weeks o
- Risk of intolerance because of possible serious drug-drug interactions
- Severe adverse drug reactions to core drugs used in regimen

Table 8.69: Constructing individualized treatment regimen (see the step wise approach below)

Steps to Design individualized MDR Treatment Regimen	
Step 1	**Choose one later generation fluoroquinolone (Levofloxacin or Moxifloxacin)** • Oflaxacin susceptibility is routinely done. In addition to ofloxacin, every attempt should be made to determine susceptibility to moxifloxacin and Levofloxacin • If only ofloxacin DST is known (and resistant) use Levofloxacin unless thought to be compromised (e.g., previous fluoroquinolone use); Moxifloxacin should be a last resort.

Step 2	**Choose both of these prioritized drugs: Bedaquiline (Bdq) and Linezolid (Lzd)** • If a drug is considered to have induced severe toxicity, do not include it in the regimen • Bdq is strongly recommended for adults >18 years, also can be used for 6–17 years.
Step 3	**Choose both of these prioritized drugs: Clofazimine, Cycloserine/terizidone** • If a drug is considered not to be effective or it has induced severe toxicity, do not include it in the regimen • If effectiveness is difficult to judge, the drug can be added to the regimen, but should not be counted as one of the effective agents.
Step 4	**Choose one of the injectables (Amikacin (Amk) or streptomycin (S)** • If a regimen cannot be assembled with five effective oral drugs outlined in step 1 to 3, and if the isolate is susceptible to the injectable, use Amikacin for adults aged >17 years. • Streptomycin is an alternative under similar conditions. Ototoxicity should be closely monitored. • If resistant to all injectable drugs, do not include injectable.
Step 5	**If needed or if oral agents preferred over injectables in Step 4,** use the following drugs: **Delamanid, Pyrazinamide, Ethambutol** • Use pyrazinamide and ethambutol only when the isolate is documented as susceptible

Step 6	**Other SL agents** • **Ethionamide (Eto) or prothionamide (Pto)** • **Imipenem–cilastatin or meropenem with clavulanate (IV route),** • **p-Aminosalicylic acid** • **High-dose isoniazid** ○ Add drugs thought to meet the criteria of an effective drug and do not induce severe toxicity ○ If effectiveness is difficult to judge, the drug can be added to the regimen, but should not be counted as one of the effective drugs. ○ Ethionamide or prothionamide and/or p-aminosalicylic acid may be included in longer regimens only if bedaquiline, linezolid, clofazimine or delamanid are not used or if better options are not possible. ○ Mutations in the inhA region of the M.tuberculosis genome can confer resistance to Eto/Pto and INH. In this situation, ethionamide/prothionamide may not be a good choice.
None	The following drugs are no longer recommended for inclusion in individualized MDR-TB regimens: Capreomycin and kanamycin; Amoxicillin/clavulanate (when used without a carbapenem); Azithromycin and clarithromycin; thioacetazone; gatifloxacin; perchlozone, interferon gamma or sutezolid

- **Extra pulmonary and central nervous system drug resistant TB**
    - The same strategy and duration of treatment as pulmonary drug-resistant TB with the only exception of CNS involvement.

- The treatment of drug resistant tuberculous meningitis should be guided by drug susceptibility results and the drugs to penetrate the central nervous system.
- The treatment duration in meningitis: a minimum of 20 months,

Table 8.70: Penetration of Anti-TB Drugs in Cerebrospinal Fluid

CNS Penetration level	Anti-TB drugs
Good penetration	Isoniazid, rifampicin, pyrazinamide, ethionamide, prothionamide, cycloserine, linezolid, imipenem, meropenem.
Penetration only through inflamed meninges	Aminoglycosides (streptomycin, kanamycin, amikacin), Fluoroquinolones (moxifloxacin, or levofloxacin,)
Poor or no penetration	Ethambutol, PAS
No or little data	Capreomycin, clofazimine, bedaquiline, Delamanid.

- **Treatment of MDR-TB in Special populations**
  - **HIV Infection**
    - Higher pill burden, drug–drug interactions, immune reconstitution inflammatory syndrome pose unique challenges Drug interactions between antiretroviral and anti-TB agents:
    - Efavirenz can produce a decrease in serum bedaquiline concentrations, avoid this combination.
    - Protease inhibitors can result in increased serum bedaquiline levels.
    - Check for overlapping toxicities and drug-drug interaction.
  - **Pregnant women**
    - Treating MDR-TB during pregnancy outweighs the harm of not treating to mother, child, and the community.

    - Most of the drugs are pregnancy category C, Bedaquiline and meropenem, are category B, and aminoglycosides are category D
    - Aminoglycosides and ethionamide can be avoided

- **Pyridoxine supplementation**
    - Pyridoxine (Vitamin B6) supplementation for all patients and for the period of the whole treatment duration.
    - For patient receiving the shorter standardized regimen: pyridoxine 25 to 50mg tablet.
    - Ptients receiving cycloserine containing regimens receive 50mg of pyridoxine for every
- **Adjunct therapy**
    - Corticosteroids
    - Beneficial as an adjunctive therapy in DR-TB patients with severe respiratory insufficiency, central nervous system or pericardial involvement.
    - Prednisone is commonly used, started at approximately 1 mg/kg of body weight with gradual tapering dosage after one to two weeks.
- **Surgery in treatment of drug-resistant TB**
    - Emergency indication: Sever hemoptysis and tension spontaneous pneumothorax.
    - Urgent indication: recurrent hemoptysis that cannot be stopped by other treatment methods.
    - Elective indications: Localized cavitary TB with positive sputum after 4-6 months, M/XDR-TB characterized by failure of anti-TB chemotherapy, local complications and sequelae
- **Monitoring patient response to MDR-TB treatment using culture**
    - Treatment response should be monitored clinically, radiographically, and bacteriologically.

  - Sputum smear microscopy and culture monthly.
  - When cultures remain positive after 3 months of treatment, do drug susceptibility tests

- **Care and support for patients with MDR/RR-TB**
  - Health education and counselling on the disease and treatment adherence.
  - One or more of the following treatment adherence interventions (complementary and not mutually exclusive) may be offered to patients
    - Tracers and/or digital medication monitor;
    - Material support to the patient
    - Psychological support to the patient
    - Staff education.
- **Treatment of Contacts Exposed to MDR-TB**
  - For close contacts with presumed MDR TB latent infection, give 6 to 12 months treatment with a fluoroquinolone alone or with a second drug, on the basis of source-case isolate DST.
  - Pyrazinamide should not be used as the second drug.

Table 8.71: Symptom based approach to the management of 2nd line Anti-TB medicines induced adverse-effects

ADR	Suspected agent	Management	Remarks
Nausea (N), vomiting (V)	Eto/Pto, PAS, H, E, Z, Cfz	1.Assess for dehydration; and rehydrate if indicated. 2. If mild symptoms and no signs of dehydration, O Advise patient to take medicines with porridge. O Initiate antiemetic therapy if needed (Metoclopromide) O Encourage patient to continue treatment O Encourage patients to increase fluid intake(water, juice, tea) 3. If there is dehydration or persistence of symptoms, ·Initiate rehydration accordingly ·Refer patient to treatment initiating center	1. N and V are very common in early weeks of therapy and usually abate with time and adjunctive therapy. 2. Electrolytes should be monitored and replaced if vomiting is severe. 3. Reversible upon discontinuation of suspected agent. 4. Clofazimine can cause severe abdominal pain and acute abdomen. This is rare, but if occurs, clofazimine should be suspended.

Gastritis	PAS, Eto/ Pto	1.Give antiTb medicines with small food, avoid caffeine, cigarettes and assess for signs of severity 2. If mild symptoms give H2-blockers, proton-pump inhibitors, or antacids. 3. If severe (severe persistent dyspepsia, hematemesis/coffee ground vomitus, black tarry stool, initiate rehydrationand refer.	1. Severe gastritis, as manifested by haematemesis, melaena or haematechezia, is rare. 2. Dosing of antacids should be carefully timed so as to not interfere with the absorption of antituberculosis medicines (take 2 hours before or 3 hours after antituberculosis medications). 3. Reversible upon discontinuation of suspected agent(s).
Hearing loss	Km,Am, Cm	1. Confirm that this is not due to ear wax or other conductive problems. 2.Check whether patient has history of hearing loss previously 3. Document hearing loss and compare with baseline audiometry if available. 4. Refer if it is new event or worsening of complaint.	1.Patients with previous exposure to aminoglycosides may have baseline hearing loss. In such patients, audiometry may be helpful at the start of MDR-TB therapy. 2. Hearing loss is generally not reversible. 3.The risk of further hearing loss must be weighed against the risks of stopping the injectable in the treatment regimen. 4.While the benefit of hearing aids is minimal to moderate in auditory toxicity, consider a trial use to determine if a patient with hearing loss can benefit from their use

Electrolyte disturbance (Low K&Mg) Manifesting as fatigue, muscle cramp, muscle spasm	Cm, Km, Am,	1. Check potassium (if available). 2. If potassium is low also check magnesium (& calcium if hypocalcemia is suspected). 3. Initiate potassium supplement if K+> 3.0meq/L) and monitor Potassium weekly 4. Correct if there are contributing causes of hypokalemia (Vomiting, diarrhea) 5. Refer if K+<3.0meq/L	1. If severe hypokalemia is present, consider hospitalization. 2. Amiloride 5–10 mg QD or Spironolactone 25 mg QD may decrease potassium and magnesium wasting and is useful in refractory cases. 3. Oral potassium replacements can cause significant nausea and vomiting. Oral magnesium may cause diarrhea.
Peripheral neuropathy	Cs, H, Km, Am, Cm, Eto/ Pto	1. Increase pyridoxine to maximum daily dose (200 mg per day). 2. Initiate therapy with tricyclic antidepressants such as amitriptyline. Non-steroidal anti-inflammatory medicines or acetaminophen may help alleviate symptoms. 3. If no improvement, refer.	1. Patients with co-morbid disease (e.g., diabetes, HIV, alcohol dependence) may be more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here. 2. Neuropathy may be irreversible; however, some patients may experience improvement when offending agents are suspended

Seizure	Cs, H, FQs	1. Suspend suspected agent pending resolution of seizures. 2. Initiate anticonvulsant therapy (e.g., Phenytoin, Valproic Acid). 3. Increase pyridoxine to maximum daily dose (200 mg per day). 4. Refer after controlling seizure	1.Anticonvulsant is generally continued until MDR-TB treatment is completed or suspected agent discontinued. 2. History of previous seizure disorder is not a contraindication to the use of agents listed here if a patient's seizures are well controlled and/or the patient is receiving anticonvulsant therapy? 3. Patients with history of previous seizures may be at increased risk for development of seizures during MDR- TB therapy a contraindication to the use of the agents listed but may increase the likelihood of depression developing during treatment.
Hypothyroidism (swelling, slowing, fatigue, day time sleepiness)	PAS, Eto/ Pto	Check TFT if available to confirm, Refer to TIC	1.Completely reversible with discontinuation of the medicine More frequent with combination medicine therapy
Blurring of vision	E, Eto	Refer	
Arthralgia	Z, FQ	1. Initiate therapy with NSAIDs (e.g Ibuprofen) 2. Refer if severe or no improvement.	

FURTHER READING

1. National guideline for TB, DR-TB and Leprosy in Ethiopia. Sixth edition. August 2018
2. WHO consolidated guidelines on drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO.

8.28 LEPROSY (HANSEN'S DISEASE)

BRIEF DESCRIPTION

- Leprosy is a chronic infectious disease caused by *Mycobaterium leprae*; mainly affecting the skin and peripheral nerves, other tissues, such as the eye, mucosa of the upper respiratory tract, joints and testis can also be involved.
- It is transmitted from person to person through the ***nasal mucosa by droplet infection*** from untreated leprosy patient to individuals living in the same household in close contact with the index case.
- It has a long incubation period, averaging 3 to 5 years, may vary from 6 months to more than 20 years.
- If not properly treated, leprosy can cause severe disability, mainly as a result of peripheral nerve damage.
- Among communicable diseases, leprosy is the leading cause of permanent physical disability.
- Usually occurs in people in the age group between 15 and 45 years.
- Fourteen (14) countries including Ethiopia represented 95% of the global leprosy burden.
- In Ethiopia, a total of 3,970 new leprosy cases (with 85% multi-Bacillary) were registered in 2015.

CLINICAL FEATURES

- The earliest clinically detectable lesion usually occurs in the skin. Patients may present with a history of any of the following complaints:
    - Pale or reddish patches on the skin with loss of, or decreased sensation on the skin
    - Painless swelling or lumps on the face and earlobes
    - Numbness or tingling of the hands and/or the feet
    - Weakness of eyelids, hands or feet, difficulty closing the eyes
    - Decreased vision
    - Burning sensation in the skin
    - Dry palms, skin cracks on palms and soles with sensation loss
    - Painless wounds or burns on the hands or feet
    - History of close contact with a leprosy patient
- **On physical examination, any of the following signs may exist**
    - Hypo-pigmented or erythematous skin lesions
    - Loss of, or decreased sensation on the skin patches when touched with a wisp of cotton
    - Enlarged/thickened peripheral nerves
    - Painful and/or tender nerves on palpation
    - Loss of muscle strength or paralysis of muscles of the eyes, hands and feet
    - Sensory loss on the soles of the feet and/or palm of the hands
    - Corneal anesthesia with loss of corneal reflex
    - Cracks on palms and soles with sensation loss
    - Wounds, ulcer on palms and soles with sensation loss

  - Clawed fingers and toes, foot drop, Wrist drop
  - Shortening and scarring of fingers and toes
- The cardinal features of leprosy are:
  - Definite loss of sensation in a pale (hypo-pigmented) or reddish skin lesion.
  - Thickened or enlarged peripheral nerve/s with or without tenderness
  - Presence of the acid-fast bacilli Mycobacterium leprae in slit skin smears from skin

Presence of one or more of the three cardinal features in Ethiopia makes the diagnosis or confirmation of a leprosy case

INVESTIGATION AND DIAGNOSIS

- Leprosy cases can be diagnosed on clinical grounds.
- Diagnosis of leprosy is confirmed when one of the three cardinal signs of leprosy present.
- Laboratory investigation is indicated for confirmation.
- Skin slit smear microscopy

CLASSIFICATION OF CASES

- A case of leprosy is classified as multi-bacilary or pauci-bacilary leprosy depending on the number of skin lesion and/or skin smear microscopy result.
  - **Multibacillary (MB) Leprosy**:
    - Usually presents with multiple (>5) poorly defined, hypopigmented or erythematous lesions associated with hypoesthesia.
    - Six or more skin lesions. Or
    - Slit skin smear result positive for AFB, irrespective of the number of skin lesion. or

  - If there is involvement (enlargement) of more than one nerve.
- **Paucibacillary (PB) leprosy:**
  - Presents with one or few (usually <5) hypopigmented and hypoesthetic lesions.
  - Only one nerve trunk enlarged and
  - Slit skin smear negative for AFB.
- **Pure neural leprosy**
  - These are patients who do not have any skin lesion, but who have clearly thickened nerves with or without signs of nerve damage.
  - Patients with pure neural leprosy should be reported and treated as a MB case

TREATMENT

OBJECTIVES

- Cure leprosy by rapidly eliminating the bacilli
- Prevent the emergence of medicine resistance
- Prevent relapse
- Prevent disability

Non pharmacologic

- Counseling and psychological support
- Socio-economic support

Pharmacologic

- Leprosy is treated with a combination of two or more medicines in the form of Multi- Medicine Therapy (MDT).
- There are virtually no relapses or recurrences of after completion of treatment with MDT.

- Patients are considered no longer infectious after taking the first dose of MDT.
- The MDT is a combination of Rifampacin, Clofazimine and/or Dapsone.
- The MDT medicines are provided in blister calendar packs each containing a four-week (one month) supply.
    - o Pauci-bacillary (PB) MDT blister pack contains Rifampicin and Dapsone
    - o Multi-bacillary (MB) blister pack contains Rifampicin, Clofazemine and Dapsone.

THE LEPROSY MULTI-MEDICINE (MDT) THERAPY REGIMEN

- There are two types of MDT regimens. The Paucibacillary (PB)-MDT and Multibacillary

(MB)-MDT:

- o Treatment of Paucibacillary leprosy
- o Rifampicin and Dapsone for 6 months (6 MDT blister packs)
    - – **Rifampicin,** 10mg/kg/day body weight **(**600mg/day for adults), supervised once-monthly x 6 months

      PLUS
    - – **Dapsone** 2 mg/kg (100mg /day for adults), daily self-administered X 6 months

Table 8.72: Dose regimens of medicines use for treatment of Pauci-bacillary leprosy

Medicines	**0-5 yrs old**	**6-14 yrs old**	**≥ 15 yrs old**
Rifampicin (4-weekly supervised)	300 mg	450 mg	600 mg
Dapsone (daily, unsupervised)	25 mg	50 mg	100 mg

- **Treatment of Multibacillary Leprosy (MB-MDT regimen)**:
  - Three drug regimen for 12 months: Rifampicin, Clofazemine and Dapsone (12 MDT blister packs).
    - **Rifampicin, 10mg**/kg (600mg P.O., for adults), once-monthly, supervised for 12 months.

    PLUS

    - **Dapsone,** 2 mg/kg (100 mg P.O., for adults), daily self-administered for 12 months

    PLUS

    - **Clofazimine,** 6mg/kg (300mg P.O., for adults) monthly, supervised and 1mg/kg (50mg for adults) daily, self-administered for 12 months.

Table 8.73: Dose regimens of medicines use for treatment of multibacillary leprosy

Drugs	0-5 yrs old	6-14 yrs old	≥ 15 yrs old
Rifampicin (4-weekly supervised)	300 mg	450 mg	600 mg
Clofazimine (4-weekly supervised)	100 mg	150 mg	300 mg
Clofazimine (unsupervised)	50 mg twice a week	50 mg q other day	50 mg daily
Dapsone (daily, unsupervised)	25 mg	50 mg	100 mg

- **Administration of MDT and Phases of Chemotherapy:**
  - Phases **of Leprosy Treatment:** MDT regimens consist two phases:
    - 1st phase (Supervised): drugs are administered under the direct observation by the health worker on fixed clinic days at four weekly intervals.
    - 2nd phase **(**Unsupervised): drugs are self-administered daily by the patient.

TREATMENT IN SPECIAL CONDITIONS

- **Patients co-infected with TB**
    - Patients suffering from both TB and leprosy require standard TB treatment.
    - Skip the monthly dose of the rifampicin in the leprosy MDT regimen during the overlapping period.
    - Once the TB treatment is completed, the patient should continue his/her MDT, or the other way round.
- **Pregnancy and breast-feeding**
    - The standard MDT regimens are safe, both for the mother, the unborn child and the child and therefore can be administered during pregnancy and breast-feeding.

MANAGEMENT OF ADVERSE EFFECTS OF DRUGS USED IN MDT

- Drugs used in MDT are generally well tolerated
- Educate the patient to anticipate some common side effects
    - Rifampicin (R): slight discoloration (reddish) of the urine and body fluids.
    - Clofazemine (C): may cause brownish discoloration and dryness of the skin. However, this disappears within few months after stopping treatment.
    - Dapsone (DDS): the main side effect is allergic reaction. Patients known to be allergic to any of the sulpha-drugs should not be given Dapsone.
- Management approach to adverse drug reaction:
    - If the patient develops minor adverse effect: Conservative management
    - If the patient develops major adverse effect: Refer to higher center for appropriate management

LEPROSY REACTIONS

- One of the most common complications in leprosy is reaction.
- Leprosy reaction is an immunological response to the bacilli, presenting as acute inflammatory episodes.
- Leprosy reactions are characterized by the sudden appearance of symptoms and signs of inflammation on the skin, eyes and peripheral nerves.
- The long-term problems related to leprosy (deformity and disability) are due to nerve damage from leprosy reactions.
- The reactions can occur before the start of treatment, during treatment and after completion of treatment.
- There are Two types of leprosy reactions
    - Reversal Reaction (Type I reaction)
    - Erythema Nodosum Leprosum (ENL) (Type 2 reaction)
- Both types are further divided into mild or severe reactions.
- Mild re**action**
    - Appears only on the skin (no major nerve or face involvement).
    - It may manifest with mild fever and slight swelling of the limbs.
    - It can be managed with rest and analgesics.
    - Usually occurs in type I reaction.
- **Severe reactions**
    - Affects the nerves or eyes
    - Require corticosteroids treatment.
    - All type II reactions are severe.
- **Mild reaction treatment**

NON-PHARMACOLOGIC

- Rest, reassurance, psychological support and counseling

Pharmacologic

- **Aspirin,** 600mg to 1200mg P.O., is given 4 to 6 times daily until the reaction is controlled and then the dose decreased gradually.

OR

- **Paracetamol**, 500 to 1000mg every 4-6 hours, maximum 4g daily
- Examine the patient after one week. If the signs persist, continue the same treatment for another week after ruling out any new nerve damage. If nerve damage observed, manage the patient as severe reaction.
- **Severe reactions**
    - Usually occurs in type 2 reaction but sometimes it can also occur in type 1 reaction. All type 2 reactions are severe
- **Severe reversal (type 1) reactions diagnosis:** if one or more of the following found
    - Pain or tenderness on palpation in one or more nerves, with or without loss of nerve function.
    - Change in voluntary muscle testing (including eye closure) < 6 months duration: from strong to weak, from weak to paralysis, or from trong to paralysis.
    - Change in sensory test < 6 months duration: any hand or foot has increased loss of sensation at two or more points.
    - A raised, red swollen patch overlying a nerve trunk or around an eye.
    - Red, raised and ulcerating skin lesions.
    - Edema of hands or feet.
    - A mild reaction persisting for a period longer than 6 weeks
- **Erythema nodosum leprosum (type 2 reaction) diagnosis**: one or more of the following

- Appearance of Erythematous sub-cutaneous nodular lesions with ulceration
- Tenderness on palpation or spontaneous pain in (a) nerve trunk(s)
- Loss of muscle strength and/or loss of sensation in eyes, hands or feet for < 6 months
- Painful eyes, with redness around the limbus cornea, increased lacrimation fixed narrowing (constriction) of the pupil and diminishing vision (irido cyclitis)
- Painful testicular swelling (orchitis)
- Painful swollen fingers (dactylitis)
- General condition: fever and malaise

- **Treatment of severe type1 reaction**
  - **Prednisone**, 1 mg/kg body weight/day (40-60mg daily), according to severity and starting high dose should be reduced to 40mg after a few days. Thereafter, the dose is reduced by 5-10mg every 2-4 weeks, ending with 10mg every 2-4 weeks (see table below).

Table 8.74: Ambulatory treatment of severe reversal reaction with Prednisolone

Duration of treatment		**Daily dose of prednisolone (do not exceed 1 mg per kg body**
MB	**PB**	
4 weeks	2 weeks	40 mg
4 weeks	2 weeks	30 mg
4 weeks	2 weeks	20 mg
4 weeks	2 weeks	15 mg
4 weeks	2 weeks	10 mg
4 weeks	2 weeks	5 mg
Total 24 weeks	**Total 12 weeks**	**Stop**

Table 8.74: Hospital treatment with Prednisolone of severe type I reaction

60 mg daily (12 tablets of 5mg prednisolone)	1 week
50 mg daily (10 tablets of 5mg prednisolone)	1 week
40 mg daily (8 tablets of 5mg prednisolone)	2 weeks
30 mg daily (6 tablets of 5mg prednisolone)	2 weeks
20 mg daily (4 tablets of 5mg prednisolone)	12 weeks
15 mg daily (3 tablets of 5mg prednisolone)	2 weeks
10 mg daily (2 tablets of 5mg prednisolone)	2 weeks
5 mg daily (1 tablet of 5mg prednisolone)	2 weeks
Total	**24 weeks**

- **Treatment of erythema nodosum leprosum (ENL) (type 2 reaction)**
    - **Prednisone**, 1 mg/kg body weight/day (60-80 mg daily) for a maximum duration of 12 weeks

Table 8.75: Four-week prednisolone treatment course for ENL

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**
Week 1	60 mg	60 mg	60 mg	60 mg	50 mg	50 mg	50 mg
Week 2	50 mg	40 mg	40 mg	40 mg	40 mg	30 mg	30 mg
Week 3	30 mg	30 mg	20 mg	20 mg	20 mg	20 mg	10 mg
Week 4	10 mg	10 mg	10 mg	5 mg	5 mg	5 mg	5mg

All patients with ENL should immediately be referred (to a hospital where experienced health workers are available) with their clinical records to hospital for treatment. Patients with ENL reaction should always be admitted as this may be a life threatening condition.

- **Treatment of Recurrent ENL**
    - A few patients get recurrent episodes of ENL as soon as the dose of prednisolone dips below 20 or 15 mg per day.
    - This is called chronic or recurrent ENL.
    - It carries the risk of prednisolone dependence and thus increases also the risks of prednisolone side effects.
    - Such patients are better co-managed with clofazimine.

Table 8.76: Treatment of recurrent ENL with clofazimine

Duration (Months)	Dose of Clofazimine
1 – 3 months	1 capsule of 100mg three times daily
3 – 6 months	1 capsule of 100mg two times daily
6 – 12 months	1 capsule of 100mg once daily

Relapse in Leprosy

- Relapse is defined as the re-occurrence of the disease at any time after the completion of a full course of treatment with MDT.
- If a full course of treatment has been administered properly, relapse is generally rare.
- Most relapses occur long after the treatment was given, sometimes more than 10 years later.
- Relapse cases can be treated effectively with the same MDT regimen as there is minimal risk of acquired drug resistance in leprosy.

Table 8.77: Differentiation between Relapse and Reactions

Criteria	Relapse	Reaction
Development of signs	Slow	Sudden
Duration after treatment completion	> 3 years	< 3 years
Site	New patches	Over old patches
Tenderness/pain	No (unless also in reaction)	Nerves usually, skin sometimes
Damage	No (unless also in reaction)	Sudden and rapid
General condition	Not affected (unless also in reaction)	Often fever, joint pain etc.
"Therapeutic trial" using steroids	No clinical improvement	Rapid clinical improvement

PREVENTION OF DISABILITY (POD) IN LEPROSY

- Most disability and deformity result directly or indirectly from loss of function of peripheral nerves supplying the eyes, hands and/or feet.
- Disability and deformity can be prevented by timely detection and prompt treatment of neuritis.
- Poor treatment of leprosy can cause permanent disability and deformity, which aggravates hopelessness, and stigma and fear against those affected.
- Interventions for Preventing Disability
  - Home-based self-care
  - Simple interventions organized at the local clinic
  - Referral for complex interventions that require specialty care

FURTHER READING

1. Federal Ministry of Health. National guidelines for TB, DR-TB and Leprosy in Ethiopia, 6th edition, August 2018.

CHAPTER 9:

KIDNEY AND URINARY TRACT DISORDERS

9.1 ACUTE KIDNEY INJURY (AKI)

BRIEF DESCRIPTION

- **Definition of AKI:** AKI is diagnosed if any one of the following criteria is fulfilled.
    - Increase in serum creatinine by > 0.3mg/dl, which is known to have occurred occur in <48 hours.
    - Increase in serum creatinine by 50% (1.5-fold) form baseline, which is known or presumed to have occurred within the prior 7 days.
    - Urine output <0.5ml/kg/hr for 6 hours (for an average adult <200ml/6 hours)
- **Staging AKI:** According to the KDIGO (Kidney Disease Improving Global Outcomes) staging, AKI is staged in to three.

Table 9.1. Staging of AKI according to KIDGO

Stages	Creatinine-based	Urine-out put base
Stage 1	Increase from baseline: 1.5–1.9 times (≥50% but <100%)	< 0.5 ml/kg/h for 6–12 hours
Stage 2	Increase from baseline 2.0 -2.9 times (>100% but < 300%)	Urine output < 0.5 ml/kg/h for >12 hours
Stage 3	Increase from baseline > 3 times (>300%) OR An increase to a level >4.0 mg/dl Or Initiation of renal replacement therapy	<0.3 ml/kg/h for ≥24 hours OR Anuria for ≥12 hour

- The causes of AKI have traditionally been divided into three broad categories:
    - Prerenal
        - Hypovolemia, Heart Failure, liver failure, altered renal autoregulation (NSAIDS, ACE inhibitors)
    - Intrinsic renal
        - Ischemic acute tubular necrosis (ATN), nephrotoxic ATN (e.g., aminoglycoside, intravenous iodinated contrast), acute glomerulonephritis, acute interstitial nephritis
    - Post renal
        - Bladder outlet obstruction, bilateral ureteral obstruction
- The cause of AKI in a single patient can be multiple (multifactorial). This particularly true in critically sick hospitalized patients.
- Whenever a diagnosis of AKI is made, the specific etiology/etiologies should be carefully searched.
- AKI is a common problem clinical problem; it is much more common in hospitalized patients than in the community.
- The common causes of dialysis requiring AKI in Ethiopia used to be severe malaria and septic abortion but recently there is a significant shift in the etiology. Hypovolemia with or without sepsis, glomerulonephritis, and obstetric causes (mainly driven by pre-eclampsia) are the leading causes.
- The elderly, diabetics, patients with underlying CKD, patients with heart failure or liver disease are at high risk of developing AKI.

CLINICAL FEATURES

- The clinical features of AKI are dominated by those of the underlying cause unless the AKI is severe.

SYMPTOMS

- Decreased urine amount.

- Fatigue
- Body swelling
- Shortness of breath
- Poor appetite, nausea and vomiting
- Hiccups
- Bleeding, mucocutaneous
- Symptoms of the underlying cause: e.g., tea/cola colored urine in glomerulonephritis, fever in sepsis/malaria

SIGNS

- Peripheral edema
- Signs of pulmonary congestion: bilateral lower lung zone crackles
- Signs of pleural effusion or ascites
- Change in mental status/flapping tremor/seizure
- Signs of pericarditis or pericardial effusion
- Signs of the underlying disease: e.g., Cutaneous and joint manifestations in SLE with glomerulonephritis, low BP and signs of dehydration in patients with pre-renal azotemia or ischemic ATN

INVESTIGATIONS AND DIAGNOSIS

Diagnosis

- The diagnosis of AKI is made based on serum creatinine and/or urine output criteria mentioned above. See the diagnostic and staging criteria above.
- Differentiating AKI from chronic kidney disease (CKD) is very important, although it might not always be straight forward.
- The presence of a previous creatinine determination helps in differentiating AKI from CKD.

- Bilateral small sized kidneys (<9cm longitudinally) indicate chronic kidney disease; however, not all patients with CKD have small size kidneys.
- Investigations
- Serum urea and creatinine
- Urinalysis
- Serum electrolytes
- Abdominal ultrasound: to exclude urinary tract obstruction and assess kidney size
- Other investigation should be done based on the suspected specific cause
- Renal biopsy: referral for renal biopsy is needed when glomerulonephritis is suspected or the cause of AKI is not clear

TREATMENT

OBJECTIVES OF TREATMENT

- Correct reversible causes of AKI
- Avoid worsening of kidney injury
- Maintain normal volume and electrolyte status
- Avoid overdoses of medications with renal clearance

Non pharmacologic treatment

1. **Maintain Fluid & electrolyte balance**
    - Strict fluid input and output chart or daily weighing
    - Decrease salt intake in fluid overloaded patients
    - Free water restriction in hyponatremia
    - Decrease foods rich in potassium
2. **Surgical intervention:** For obstructive uropathy
3. **Prevent further kidney injury**

  - Avoid nephrotoxic medications and radiocontrast agents
  - Adjust doses of medicines with renal clearance
  - Treat Heart Failure

4. **Dialysis**: if the patients live far from a hospital with dialysis service, referral should be made before the indications for dialysis develop.
  - **Indications for dialysis**
    - Pulmonary edema and anuria.
    - Intractable metabolic acidosis.
    - Severe hyperkalemia (> 6.5 mmol/l).
    - Uremic complications-pericarditis, encephalopathy and bleeding

PHARMACOLOGIC TREATMENT

- There is no specific pharmacologic treatment for AKI caused by ischemic or nephrotoxic acute tubular necrosis.
- The specific treatment depends on the cause of the AKI.
- **Intravenous fluids**
  - Indicated only in patients are who are hypotensive or dehydrated on clinical evaluation.
  - In patients with hypovolemia or clinical hydration, fluids should be given to keep the fluid balance in the positive side.
  - Do not give ("challenge') fluid for all patients unless there is evidence of volume depletion)
  - Urine output and fluid balance should closely be followed as oliguric patients can easily develop pulmonary edema.
- **Furosemide**:
  - Indicated in patients with signs of fluid overload (edema, evidence of pulmonary congestion or high BP)

  - Starting dose 40mg, intravenously. If no response increases the dose every 1-2 hour till adequate response.
  - Do not go beyond 200mg/dose.
  - Doses above 100mg should be given diluted (1-2mg/ml of fluid) and given slowly (4mg/min).
    - E.g., 200mg in 100ml NS/01 hr, 160mg in 100mL NS/ 40min
  - Response can be considered adequate, if the urine output is 50-100ml in 01 hour, or 100-200ml in 02 hours.
- **Treatment of hyperkalemia**-see section on hyperkalemia
- **Treatment of hypertensive emergency**-see section on hypertension
- **Treatment of specific cause**: depends on the cause depends. E.g.

Prevention

- A significant proportion of AKI is preventable.
  - Rapid and adequate fluid replacement in volume depleted patients
  - Early detection and management of sepsis, malaria, pre-eclampsia
  - Avoiding nephrotoxic medications in high-risk patients, whenever possible e.g., NSAIDS, aminoglycosides, iodinated intravenous contrast agents.
  - Close monitoring of renal function and urine output in hospitalized patients
  - Dose adjustment of drugs with renal clearance.

REFERRAL

- The following patients with AKI need to be referred to a hospital with a nephrology and dialysis services without delay.
  - Worsening AKI despite efforts to manage the possible causes
  - Glomerulonephritis considered to be the cause of AKI

  - AKI of unknown etiology
  - Any indications for dialysis

FURTHER READING

1. Peter K. Moore, Raymond K. Hsu, and Kathleen D. Liu. Management of Acute Kidney Injury: Core Curriculum 2018. Am J Kidney Dis. 72(1):136-148.
2. KDIGO Clinical Practice Guideline for Acute Kidney Injury Kidney International Supplements (2012) 2, 1; doi:10.1038/kisup.2012.

9.2 CHRONIC KIDNEY DISEASE (CKD)

BRIEF DESCRIPTION

- Chronic Kidney disease is defined as the presence of kidney damage for more than three months as evidenced decreased glomerular filtration rate of < 60m/min or the presence of other markers of kidney damage with or without decreased GFR
- Other makers of kidney damage;
  - Abnormalities on urinalysis: Persistent proteinuria is the most important one.
  - Abnormalities on imaging: shrunken kidneys, polycystic kidneys, hydronephrosis.
  - Histologic abnormalities findings on renal biopsy specimens
- For determination of estimated GFR in adult patients with stable serum creatinine, use the MDRD or CKD-EPI formula, which are freely accessible on line.
- The commonest causes of chronic kidney disease are: hypertension, diabetes mellitus, glomerulonephritis, polycystic kidney disease and obstructive uropathy.
- End stage renal disease (ESRD) – refers to a state of advanced CKD with

estimated GFR being < 15ml/min where lifelong renal replacement therapy (dialysis or kidney transplantation) is necessary to sustain a reasonable quality of life and survival.

CLINICAL FEATURES

Symptoms

- Generally asymptomatic in the early stages
- As CKD advances some non-specific symptoms might develop
- Common but non –specific symptoms:
    - Nocturia
    - Fatigue
    - Loss of appetite, nausea, vomiting, hiccup
    - Weight loss
    - Muscle cramps, paresthesia
    - Pruritus
    - Body swelling, shortness of breath
    - Sleep disturbance, depression, anxiety, sexual dysfunction

SIGNS

- There are specific signs for CKD.
- Early stages of CKD might not have any signs apart from signs of the underlying disease
- Advanced stages
    - Edema, pleural effusion or crackles on lower lung field
    - Dry skin, excoriation marks, papular eruptions, uremic frost
    - Pericardial friction rub or distant heart sounds
    - Uremic fetor, decrement in cognition, flapping tremor, lethargy

Table 9.2. Staging of Chronic kidney disease based on CAG (cause, albuminuria and GFR)

Staging based on GFR (G)	**GFR (ml/min)**
G1	>90
G2	60-90
G3a	45-59
G3b	30-44
G4	15-29
G5	<15

Staging by albuminuria or proteinuria (A)	**24hr urine albumin (mg)**	**24hr urine protein (mg)**
A1	< 30	<150
A2	30-300	150-500
A3	>300	>500

CAUSE (C):

1. Determine possible cause by taking history, physical examination and doing relevant investigations.

○ Diabetes - Hypertension - Autoimmune diseases

○ Primary glomerular disease - Obstructive uropathy

○ - Polycystic kidney disease

INVESTIGATIONS AND DIAGNOSIS

Diagnosis

- The diagnosis is of CKD is made based on the KDIGO criteria mentioned above.
- Once the diagnosis of CKD is established cause identification and staging should be made based on the CAG system (C-cause A-albuminuria level

and G-GFR level).

- Example if a patient with CKD presumed to be due to diabetic kidney disease has eGFR of 40m/min and 24hr protein is 1200mg.

  C= Diabetes G=G3b A= A3 (Stage: G3b A3 CKD due to diabetic kidney disease)

INVESTIGATIONS

- Serum creatinine and urea: Estimated GFR
- Urinalysis
- Quantification of proteinuria or albuminuria: 24urine protein/albumin, spot urine albumin to creatinine ratio (ACR)
- Abdominal ultrasound
- Calcium, Phosphate, PTH levels (preferably intact PTH level than total PTH)
- Alkaline phosphatase
- Serum electrolytes
- Abdominal ultrasound
- CBC

Estimated GFR (eGFR) should be used for follow up of patients with CKD than serum creatinine alone

TREATMENT

Objectives of treatment

- Slow the progression of decline in GFR
- Prevent, detect and manage complications
- Improve quality of life and survival
- Non pharmacologic

- General health advice e.g., smoking cessation, weight reduction for obese individuals
- Restrict salt intake
- Dietary protein reduction
  - Physicians should not overemphasize on protein restriction as the benefits are modest.
  - In malnourished individuals, which many advanced CKD patients are, protein restriction should not be advised.
- Renal replacement therapy (RRT) for ESRD: Dialysis and kidney transplantations are the options
  - Renal transplantation is the preferred modality of RRT
  - Preemptive kidney transplantation is preferable (Before initiating dialysis)
- Indications for RRT
  - For preemptive kidney transplant: patients with GFR <20ml/min are candidates
  - For dialysis
    - Patients with GFR<15ml/min and symptomatic
    - Starting dialysis based on low GFR alone without symptoms is not beneficial.

PHARMACOLOGIC TREATMENT

1. Treatment and control of hypertension

- **Target blood pressure < 130/80 mmHg**
- **First line: ACE inhibitors or angiotensin receptor blockers (ARBs)**…see section on hypertension for the options.
  - Avoid ACE inhibitors/ARBs if patient has hyperkalemia.
  - Serum creatinine and potassium should be followed one to two

weeks following initiation or dose increment.

- If serum potassium or creatinine can't be followed, don't start ACE inhibitors/ARBs in patients with CKD.
- Up to 20-30% increment in creatinine is expected; hence, if the rise in creatinine is less than 30%, the ACEi/ARB needs to be continued with close monitoring. If the increase is above 30% or <30% but progressively increasing, the drug should be discontinued.

○ **Add-on and Alternatives**

- If BP is not controlled to the target with ACE inhibitors/ARBs or ACE inhibitors are contraindicated, add or replace by other antihypertensive.
- Long-acting **calcium channel blocker (CCB)**: Amlodpine or sustained/extended release Nifedipine

OR

- **Loop diuretics** (if eGFR is ≤30m/min) or **thiazide diuretics (if GFR>30ml/min)**

OR

- A combination of long-acting calcium channel blocker and diuretics (loop or thiazide, based on the eGFR)
- If the above three (ACEi/ARB + CCB + diuretic) or two (CCB + Diuretic) fail achieve target BP add **a beta-blocker.**

2. **Treatment and control of proteinuria**

○ **First line**

- ACE inhibitors or angiotensin receptor blockers (ARBs).
- **ACE inhibitors** (particularly Enalapril) are preferred over ARBs due to their low cost and wide availability.
    - ✓ **Enalapril:** starting dose 5mg BID, Maximum dose 20mg BID…**First line**

ALTERNATIVES

- ✓ **Lisinopril:** starting dose 5mg/day, Maximum dose 40mg/day
- ✓ **Perindopril:** starting dose 5mg/day. Maximum dose 15mg/day
- ✓ **Telmisartan:** Starting dose: 40mg/day maximum dose 80mg/day
- ✓ **Irbesartan:** Starting dose: 75-150mg/day, maximum dose 300mg/day
- ✓ **Losartan:** Starting dose 50mg/day maximum dose 100mg/day
- ✓ **Valsartan:** Starting dose 80 -160mg/day, maximum dose 320mg/day
- ✓ **Candesartan:** Starting dose 8-16mg/day maximum dose 32mg/day

3. Control of hyperglycemia in Diabetes

- ○ In early CKD good blood sugar control is essential and helps to decrease progression of CKD.
- ○ In advanced CKD (Stage G4 and above or in patients on dialysis) the risk of hypoglycemia is very high and tight glycemic control should be avoided.
- ○ Although individualization based on age, expected survival, rates of hypoglycemia, additional comorbidities is need, in patients with eGFR<30ml/min a HbA1C target of about 7.5% is acceptable (if achieved without significant hypoglycemia)
- ○ In patients with advanced CKD eGFR <30ml/min
  - – Metformin should be discontinued.
  - – Long-acting sulfonylureas (particularly the commonly used Glibenclamide) should be avoided.

  - Insulin based therapy is preferred.

4. Treatment of anemia of CKD

- Indications to start treatment: Hemoglobin < 10g/dl or symptomatic.

- **Iron**
  - Serum iron studies: Ferritin and transferrin saturation (TSAT) (TSAT= Serum iron ÷ TIBC x 100%) helps to guide iron therapy.
  - TSAT < 20% should be treated with iron.
  - If iron studies cannot be done, most patients with CKD are iron deficient and should be started on therapeutic iron.
  - Ferritin can be high even in iron deficient CKD patients; hence high ferritin should not be a reason to differ iron.

- **Preferred: Intravenous iron**
  - **Iron** sucrose
  - For **patients not on hemodialysis:**
    - **Iron sucrose 200mg, IV**, administer over 5 minutes, every 3 days for a total of 5 doses (a total of 1000mg). This dose is usually sufficient but if hemoglobin is not corrected, additional doses can be given.

      OR

    - **Iron sucrose** 200mg diluted in 100ml NS; administer over 30 minutes.
  - **For patients on hemodialysis**
    - **Iron sucrose** 100mg, IV, over 2-5 minutes, given early during dialysis sessions (within the first hour) until iron deficiency is corrected. It needs to be given again, if iron deficiency persists or recurs.

- **Alternative: Options**

- **Ferrous sulfate,** 325mg (65mg elemental iron) before meal

  OR

- **Ferrous gluconate**, 325mg P.O. (39mg elemental iron), 1-2tabs, TID

  OR

- **Ferrous fumarate**, 325mg P.O., (107 elemental iron), one tab, daily to twice per day.

- For patients who do not tolerate ferrous sulfate tablets, they may be advised to take it with meals, or to take a smaller dose, or elixir (solution) forms.

- **Iron hydroxide polymaltose syrup** (Each 5ml contains 50mg elemental iron), 10ml PO, BID to TID.

  OR

- **Ferrous gluconate syrup** (Each 5ml contains 24mg elemental iron), 15ml, PO TID.

  OR

- **Ferric ammonium citrate syrup (**Each 15ml contains 32.8mg elemental iron), give 30ml, TID.

5. **Erythropoiesis stimulation agents (ESA):**

- **Epoetin (alpha/beta)**
  - Initiate if Hemoglobin is < 10g/dl after iron therapy.
  - CKD patients on hemodialysis
  - Initial dose: 4000IU, IV, 3 times a week
  - CKD patients not on dialysis
  - Initial dose: 4000IU, SC, 3 times a week
  - Dosage **adjustments for CKD patients** (either on dialysis or not on dialysis):

  - Do not increase dose more frequently than every 4 weeks (dose decreases may occur more frequently).
  - If hemoglobin does not increase by >1 g/dl after 4 weeks: Increase dose by 25%
  - If hemoglobin increases >1 g/dl in any 2-week period: Reduce dose by 25-50%

- **Treatment of hyperphosphatemia:** Phosphate binders are indicated if serum phosphorus is > 5.5mg/dl
- **First line**
  - **Sevelamer** (as hydrochloride or carbonate)
  - Initial dose 800mg, PO, TID with meal. If serum phosphorus >9mg/dl, 1600mg, PO TID can be started.
  - Adjust the dose to target to a target serum phosphorus near normal (< 5.5mg/dl)
- **Alternative:**
  - Calcium carbonate: starting dose 500 – 1000mg, PO, TID, chew, with meal
  - Calcium acetate: starting dose 1334mg, PO, TID with meal
  - If total serum calcium increase >10mg/dl: hold calcium
  - If there is hypocalcemia, calcium-based phosphate binders are preferred over sevelamer.
- **Treatment of secondary hyperparathyroidism**
  - The main stay of treatment is correcting phosphorus and serum calcium
  - Serum PTH (preferably intact PTH) should not be overcorrected: 2-9 times the upper limit of normal is acceptable.
  - If PTH level is above nine times the upper limit after correction of phosphorus and calcium uses either of the following: Calcitriol or synthetic vitamin D analog (alfacalcidol or paricalcitol).

- **Alfacalcidol:** starting dose 2.5 to 5 microgram/day.

  OR

- **Paricalcitol**: starting dose 1microgram/day or 2 microgram 3x/week.

  OR

- **Calcitriol**: 0.25 – 0.5 microgram/day

- **Treatment of fluid overload (edematous state)**
  - Furosemide, 40-120mg, PO/IV, two –three times per day.
  - Higher dose and more frequent dosing intervals are required in advanced CKD.

- **Treatment of hyperkalemia**-see section on electrolyte abnormalities, sub-section hyperkalemia

FURTHER READING

1. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements (2013) 3, 1; doi:10.1038/kisup.2012.73
2. Teresa K. Chen, Daphne H. Knicely, and Morgan E. Grams. Chronic Kidney Disease Diagnosis and Management A Review. JAMA. 2019;322(13):1294-1304.
3. David Y. Gaitonde, David L. Cook, and Ian M. Rivera. Chronic Kidney Disease: Detection and Evaluation. Am Fam Physician. 2017;96(12):776-783

9.3 ELECTROLYTE ABNORMALITIES

9.3.1 POTASSIUM DISORDERS

9.3.1.1 HYPOKALEMIA

BRIEF DESCRIPTION

- Hypokalemia is defined as serum potassium level less than 3.5mmo/l.
- A serum K+ level <2.5 mmol/l is regarded as severe hypokalemia and a level of 2.5-3.0 mmol/l is considered moderate.
- Hypokalemia is either caused by loss from the body or entrance (shift) of the plasma potassium in to the cell (intracellular compartment)
  - **Causes due to potassium loss**
    - Renal loss: Diuretics, DKA, resolving AKI/obstructive uropathy, prolonged vomiting or NG tube drainage)
    - Renal loss: Hypomagnesemia, renal tubular disorders due to drugs like aminoglycosides, amphotericin, tenofovir, inherited tubular diseases
    - Renal loss: hyperaldosteronism
    - GI loss: diarrhea
  - **Causes due to redistribution/shift into intracellular space**
    - Medicines: Insulin, beta-2 agonists
    - Metabolic alkalosis

CLINICAL FEATURES

Symptoms

- Unless it is severe, hypokalemia is generally asymptomatic.
- If there are symptoms attributable to hypokalemia, it is considered to be severe.

- Symptoms of muscle weakness:
    - Weakness of extremities
    - Abdominal distention and failure to pass feces due to paralytic ileus
    - Rarely features of rhabdomyolysis: muscle weakness, pain and dark urine

SIGNS

- Mild to moderate hypokalemia does not cause signs
- Decreases muscle power
- Gaseous abdominal distention with decreased to absent bowel sounds
- Arrhythmias: the most feared manifestation of hypokalemia is ventricular arrhythmia, as it is sudden onset there might not be any signs during evaluation

INVESTIGATIONS AND DIAGNOSIS

Diagnosis

- The diagnosis is made based of serum potassium determination.
- ECG is needed to assess the severity

Investigations

- Serum potassium
- Serum magnesium
- ECG
- Further investigations to determine the underlying cause might be needed if the cause is not obvious

TREATMENT

Objectives of treatment

- Prevent and treat life-threatening complications (arrhythmias and paralysis)

- Correct potassium deficit
- Prevent ongoing potassium deficit
- Treat the underlying cause

NON PHARMACOLOGIC TREATMENT

- Encourage foods rich in potassium e.g., Peanut butter, avocado, bananas, orange juice, papaya.
- Avoid exercise in patients with moderate to severe hypokalemia

Pharmacologic treatment

- **Severe hypokalemia**
  - **Potassium chloride** (KCl) IV infusion. 40-60 meq of elemental potassium, in 1000ml Normal saline, to run every 6-8 hours.
    - Use non dextrose containing fluids
    - Maximum concentration of potassium is 60meq in one liter of fluid
    - Maximum rate of infusion (in the presence of perfuser machine) is 10meq/hour

PLUS

  - **Potassium chloride** (KCl) tablet, 600mg (equivalent to 8meq of potassium), PO, 2-3tabs, 3-4 times/day.

- **Mild to moderate hypokalemia**
  - **Potassium chloride** (KCl) tablet, 600mg (equivalent to 8meq of potassium), PO, 2-3tabs, 3-4 times/day.
  - For Hypokalemia due chronic loop diuretics: Spironolactone-see doses in each indication (Heart Failure, liver cirrhosis)
- **Treatment of the cause**
  - Some causes of hypokalemia may be treated pharmacologically. See the examples below.

  - Vomiting - anti-emetics
  - Hypomagnesemia - magnesium sulfate
  - Hyperaldosteronism (Aldosteronism)- spironolactone
  - Potassium wasting tubulopathies - spironolactone or NSAIDS.

REFERRAL

- Patients with chronic hypokalemia the cause of which is not established need to be referred to a hospital with nephrology service.

FURTHER READING

1. Anthony J. Viera and Noah Wouk. Hypokalemia and Hyperkalemia. Am Fam Physician. 2015;92(6):487-495.
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3. Efstratios Kardalas, Stavroula A Paschou, Panagiotis Anagnostis, Giovanna Muscogiuri et al. Hypokalemia: a clinical update. Endocrine Connections (2018) 7, R135–R146.

9.3.1.2 HYPERKALEMIA

BRIEF DESCRIPTION

- Hyperkalemia is defined as a serum potassium level of > 5.5mmol/l.
- It is considered severe if the serum potassium is >6.5mmo/l or there is ECG or clinical manifestation associated with the hyperkalemia.
- A decrease in renal K+ excretion due to acute or chronic kidney disease is the most common underlying cause.
- Causes of hyperkalemia
  - **1. Low renal excretion**: AKI or CKD
  - **2. Low renal excretion**: spironolactone, ACE inhibitors/ARBS,

NASAIDS, adrenal insufficiency

- ○ **3. Excess intake:** potassium tablets, potassium rich diet in patients with AKI/CKD
- ○ **4. Release from intracellular space**: tumor lysis, rhabdomyolysis, hemolysis
- ○ **5. Shift from intracellular space**: acidosis, digoxin, adrenergic blockers
- ○ **6. Pseudo hyperkalemia** (In-vitro cell death): tight tourniquet, thrombocytosis, erythrocytosis, marked leukocytosis

CLINICAL FEATURES

- Mild hyperkalemia is generally asymptomatic
- Severe hyperkalemia results in muscle weakness or paralysis, cardiac conduction abnormalities and cardiac arrhythmias.

Investigations and diagnosis

DIAGNOSIS

- The diagnosis is made based of serum potassium determination.
- If there is no obvious cause, pseudohyperkalemia needs to be excluded
- ECG is needed to assess the severity.

INVESTIGATIONS

- Serum potassium
- Serum creatinine and urea
- ECG
- Investigations for causes e.g., if adrenal insufficiency is suspected basal serum cortisol level will be needed for screening purpose.

TREATMENT

OBJECTIVES OF TREATMENT

- Prevent cardiac arrhythmias
- Maximize potassium loss
- Enhance transcellular shift from the extracellular space to intracellular space

NON PHARMACOLOGIC TREATMENT

- Decrease food rich in potassium-see section on hypokalemia
- Discontinue medicines which increase potassium-ACEIs, ARBs, Spironolactone, NSAIDs
- Dialysis: in refractory hyperkalemia due to AKI or CKD/ESRD

PHARMACOLOGIC TREATMENT (FOR SEVERE HYPERKALEMIA)

- **Calcium gluconate,** IV, 10ml of a 10% solution, over two to three minutes, with constant cardiac monitoring. The dose can be repeated after five minutes, if the ECG changes of hyperkalemia persist or recur

PLUS

- **Regular Insulin**, 10 units IV, followed immediately by 60-80ml ml of 40% dextrose (25g of glucose), every 4-6 hours

PLUS

- **Salbutamol**, 10 to 20mg in 4 mL of saline by nebulization over 10 minutes or metered Dose Inhaler or MDI 100mcg/puff-8 to 10 puffs every 20-30 minutes.

PLUS

- **Furosemide, 40-120mg**, IV, -dose should depend on previous response, degree of kidney function impairment. The dose can be repeated according to response.

REFERRAL

- Patients in whom the cause of potassium disorder is not clear need to be referred to a hospital with renal service.

FURTHER READING

1. Anthony J. Viera and Noah Wouk. Hypokalemia and Hyperkalemia. Am Fam Physician. 2015;92(6):487-495.
2. Miriam Zacchia, Maria Luisa Abategiovanni, Spiros Stratigis, Giovambattista Capass. Potassium: From Physiology to Clinical Implications. Kidney Dis 2016; 2:72–79.
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9.3.2 SODIUM DISORDERS

9.3.2.1 HYPONATREMIA

BRIEF DESCRIPTION

- Hyponatremia is defined as a plasma sodium concentration of <135mmol/L. Severe hyponatremia is defined as a plasma sodium concentration of <115mmol/L
- Acute hyponatremia is development of hyponatremia in < 48 hours.
- Hyponatremia can be due to a gain of water in excess of sodium, a loss of sodium in excess of water or both.
- Causes of hyponatremia-classified based on the volume status of the patient
    1. **Hypovolemic hyponatremia**-diarrhea, vomiting, burn, polyuria
    2. **Euvolemic hyponatremia**-syndrome of inappropriate ADH secretion (SIADH), hypothyroidism, low dietary solute intake
    3. **Hypervolemic Hyponatremia**-Heart failure, kidney failure, liver failure, nephrotic syndrome.

CLINICAL FEATURES

- **Acute hyponatremia (duration known to be <48 hr.)**

  - Seizures
  - Confusion and disorientation
  - Coma
  - Respiratory distress
- **Chronic hyponatremia (duration known to be >48 hr.)**
  - Frequently mild or no symptoms

INVESTIGATIONS AND DIAGNOSIS

DIAGNOSIS

- The diagnosis of hyponatremia is made based on the serum sodium level.
- Clinical evaluation is needed to classify the volume status of the patient and the more specific cause.

Investigation

- Serum electrolytes
- Creatinine and BUN
- Chest X-ray: If pulmonary pathologies (pneumonia, lung cancer) suspected.
- Thyroid function test: In euvolumic hyponatremia
- Serum cortisol: basal or random (in critical patients)
- Investigation directed to the suspected underlying cause

TREATMENT

OBJECTIVES OF TREATMENT

- Restore plasma tonicity
- Prevent serious CNS complications
- Avoid rapid correction
- Detect and correct the underlying cause

NON PHARMACOLOGIC TREATMENT

- Free water restriction – for euvolemic and hypervolemic causes
- Encourage table salt intake-if not hypervolemic
- Discontinue thiazide diuretics
- Management of the underlying cause

PHARMACOLOGIC TREATMENT

- Hypovolemic hyponatremia
    - **Normal saline**, IV infusion-volume depending on the estimated fluid deficit
- Hypervolemia hyponatremia
    - **Furosemid**e, dose depending on the underlying disease and previous response.
- Euvolemic hyponatremia: if it is severe/symptomatic acute hyponatremia
    - **3% NaCl** (513mmol of Na/L), 1-2 ml/kg IV per hour
    - Should elevate the serum Na approximately 1-2mmol per hour
    - Raising the serum Na 4-6mmol/L over 2-3 hours is enough to prevent serious neurologic complications
    - Subsequently, the rate of correction should be less than 10mmol/L per 24 hour.

1. As hypertonic saline is not commonly available, some practitioners advise patients to take more salt or an arbitrary amount of salt. This practice could be dangerous as it might result in overcorrection.
2. The following could serve as an improvised guidance on preparing 3% NaCl oral solution
   - 1 tea spoon (tsp)of table salt = 6 g salt ≈ 2,400 mg sodium = 104 mmol sodium
   - A 500ml of standard 3% saline (3% hypertonic saline) contains 256.5mmol of sodium
   - To prepare as 500ml of 3% sodium chloride solution, **add 2 and a ½ tsp (tea spoon of salt in 500ml of water.**
   - Example of administration: For a 70kg male adult with an aim to increase serum sodium by 8mmmol/24 hour, give 35ml of the about solution every hour. (This should be given by measuring the amount using a syrine)

FURTHER READING

1. Goce Spasovski1, Raymond Vanholder, Bruno Allolio, Djillali Annane et al. Clinical practice guideline on diagnosis and treatment of hyponatremia. Nephrol Dial Transplant (2014) 29 (Suppl. 2): ii1–ii39.

2. Ewout J. Hoorn and Robert Zietse. Diagnosis and Treatment of Hyponatremia: Compilation of the Guidelines. J AmSoc Nephrol 28: 1340–1349, 2017.

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9.3.2.2 HYPERNATREMIA

BRIEF DESCRIPTION

- Hypernatremia is defined as plasma sodium concentration of >145mmol/l.
- Severe hypernatremia is plasma sodium value of >160 mmol/L.
- Hypernatremia can be due to loss of water, gain of sodium, or both. Loss of water is the more common denominator.
- Individuals who can get and take water are unlikely to develop hypernatremia. Hence, he majority of patients who develop severe hypernatremia are patients who cannot get water by themselves e.g., patients with depressed mental status, stroke, on mechanical ventilator, the very elderly.
- Hypernatremia leads to shrinkage of brain cell volume and secondary neurological symptoms
- **Causes of hypernatremia**

1. Hypovolemic hypernatremia

- Renal water loss
    - Loop diuretics
    - post obstructive dieresis
    - osmotic diuresis
- Extra renal water loss:
    - Burns
    - Diarrhea

2. Euvolemic hypernatremia: Diabetes insipidus, hypodipsia

3. Hypervolemic hypernatremia: Iatrogenic (sodium bicarbonate, hypertonic saline),

CLINICAL FEATURES

- Mild and chronic hypernatremia is usually asymptomatic

- If conscious most patients with hypernatremia will have excessive thirst
- Severe acute hypernatremia causes CNS symptoms-irritability, lethargy, seizure and coma.

INVESTIGATIONS AND DIAGNOSIS

Diagnosis

- Diagnosis is made based on serum sodium determination

Investigation

- Serum electrolytes
- Creatinine and BUN
- Urine specific gravity/osmolality
- Blood sugar
- If diabetes insipidus is suspected refer to next level of care after management of the acute state.

TREATMENT

OBJECTIVES OF TREATMENT

- Correction of water deficit and restoration of serum tonicity
- Avoid rapid correction.
- Detection and treatment of the underlying cause

NON PHARMACOLOGIC TREATMENT

- Encourage free water intake for thirst. This is the preferred route of correcting water deficit in conscious patients with intact thirst.

PHARMACOLOGIC TREATMENT

- The main stay of treatment for hypernatremia is water (free water) given orally (preferred) or intravenously as 5%DW but the patients volume status
- Depends on the severity of hypernatremia and the patient's volume state.

- **Hypovolemic Hypernatremia:**
  - Intravenous **Ringer's lactate** until hypovolemia improves.
  - Once the hypovolemia improves shift the fluid to 5%DW after calculating the water deficit.
- **Euvolemic Hypernatremia:**
  - Correct water deficit using either oral free water or 5%DW
  - Replace ongoing losses
  - Refer to specialist if Diabetes Insipidus is suspected.
- **Hypervolemic Hypernatremia:**
  - **Thiazide** diuretics are preferred if the volume overload is mild

    Alternative
  - **Furosemide** IV or P.O., dose and route depending on severity of hypervolemia.

- **Rate of correction of hypernatremia**
  - In acute hyponatremia (developing within hours) immediate reduction of serum Na is recommended but at a rate not exceeding **0.5mmol/hour over 48-72 hours**.
  - Correction should not exceed **10mmol/day.**
- **Calculation of water deficit**
  - **Water deficit = CBW x [(serum Na) ÷ 140) - 1]**
    - CBW refers to estimated current body water
    - CBW = 60 and 50% body weight in younger men and women, respectively
    - CBW= 50 and 45% in elderly men and women, respectively.

REFERRAL

- Patients suspected of having diabetes insipidus (with polyuria, polydipsia, dilute urine and no diabetes mellitus) should referred for specialist evaluation.

FURTHER READING

1. N. Winn Seay, Ruediger W. Lehrich, and Arthur Greenberg. Diagnosis and Management of Disorders of Body Tonicity—Hyponatremia and Hypernatremia: Core Curriculum. AJKD Vol 75 | Iss 2 | February 2020.
2. George Liamis, Theodosios D. Filippatos & Moses S. Elisaf (2016) Evaluation and treatment of hypernatremia: a practical guide for physicians, Postgraduate Medicine, 128:3,299-306
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9.3.3 CALCIUM DISORDERS

9.3.3.1 HYPERCALCEMIA

BRIEF DESCRIPTION

- Hypercalcemia is defined as a total serum calcium >10.3mg/dl or an ionized calcium >5.2mg/dl (2.6mmol/l)
- Total calcium should always be corrected for serum albumin.
- Corrected calcium= measured calcium + [0.8 x (4.0- serum albumin)]
- The most important denominator in the causation of hypercalcemia is increased bone resorption. The contribution of increased oral absorption is modest.
- The two most common causes of hypercalcemia primary hyperparathyroidism and malignancy accounting 90 percent of cases.
- The work up of hypercalcemia is focused on differentiating the two (primary hyperparathyroidism
- Other less common causes include

  - Increased vitamin D activity: excess ingestion, overproduction in granulomatous diseases (tuberculosis, sarcoidosis)
  - Decreased renal excretion: Familial hypocalciuric hypercalcemia
  - Tertiary hyperparathyroidism: in advanced CKD
  - Endocrinopathies: hyperthyroidism, adrenal insufficiency
  - Drugs: thiazide diuretics, Lithium
  - Excess calcium intake
- Mild= 10.3- 12mg/dl Moderate= 12-14 Severe >14mg/dl

CLINICAL FEATURES

Symptoms and signs

- Mild hypercalcemia is generally asymptomatic
- Symptom develop if severe hypercalcemia develops over a shorter period of time
- Symptoms are remembered as "Stones, bones, moans and groans".
- Bone pain
- Fatigue, muscle weakness
- Polyuria, polydipsia, kidney stones
- Constipation, anorexia, nausea, vomiting, constipation, pancreatitis
- High blood pressure
- Anxiety, depression, cognitive dysfunction
- Confusion and coma

INVESTIGATION AND DIAGNOSIS

Diagnosis

- Once hypercalcemia is confirmed from serum total calcium or ionized calcium, the next step important investigation is determination of serum PTH.

- Low PTH: very likely hypercalcemia due to malignancy or vitamin D related causes
- High or normal PTH: Hyperparathyroidism
- If serum PTH can't be done and the patient has overt malignancy, consider the hypercalcemia to be due to the malignancy.
- Investigations
- Other investigation for patients with low serum PTH
    - Investigate for malignancy based on clinical clues e.g., screening for multiple myeloma
    - Serum 25(OH) and 1,25(OH)Vitamin D
- Phosphorous: low in primary hyperparathyroidism, elevated in Vitamin D related causes
- ECG: short QT interval
- X-rays: osteoporotic changes in cortical bone, typically in the wrist, bone cysts (osteitis cystica firbrosa) in the long bones
- Ultrasound: Renal stones or evidence of ne

TREATMENT

OBJECTIVES OF TREATMENT

- Increase renal excretion
- Decrease mobilization of calcium from the bone
- Treat the underlying cause

NON-PHARMACOLOGIC TREATMENT

- If the patient has severe hypercalcemia (>14mg/dl) or has severe symptoms (features of dehydration, change mental status) urgent admission is needed.
- Discontinue drugs which can cause hypercalcemia: thiazide, lithium
- Surgical management: in primary hyperparathyroidism, if there are indications.

PHARMACOLOGIC TREATMENT

- **Severe hypercalcemia**

1. **Aggressive hydration with normal saline** for few days
    - ○ 4-6 liters of NS over 24 hours (1liter over 4-6 hours), close monitoring for fluid overload and fluid balance.
    - ○ Do not routinely use Furosemide unless the patient is fluid overloaded (pulmonary crackles, raised JVP).
    - ○ If Fluid overloaded, 20-40mg IV, when needed. Similar doses of can be repeated if fluid overload persists.
2. **Intravenous bisphosphonate**
    - ○ **Zolendronic acid 4mg,** diluted in 100ml of NS or D5W, given as infusion over 15-30minutes.
3. **Corticosteroids**
    - ○ **Dexamethasone** 4mg IV BID

      OR
    - ○ **Hydrocortisone** 100mg IV every 12hour

      OR
    - ○ **Prednisolone** 30-40mg/day.

REFERRAL

- All patients with moderate or severe hypercalcemia should be referred urgently after correction of severe hypercalcemia.
- Patients with mild hypercalcemia should also be referred to referral hospitals on elective basis.

FURTHER READING

1. Salvatore Minisola, Jessica Pepe, Sara Piemonte, Cristiana Cipriani. The diagnosis and management of hypercalcaemia. BMJ 2015;350:h2723 doi: 10.1136/bmj.h2723.

2. Amanda DeMauro Renaghan and Mitchell H. Rosner. Hypercalcemia: etiology and management. Nephrol Dial Transplant (2018) 33: 549–551doi: 10.1093/ndt/gfy054

3. Jennifer Walsh, Neil Gittoes, and Peter Selby. Society for Endocrinology Endocrine Emergency Guidance. Emergency management of acute hypercalcemia in adult patients. Endocrine connections 3 August 2016. http://www.endocrineconnections.org. DOI: 10.1530/EC-16-0055.

9.3.3.2 HYPOCALCEMIA

BRIEF DESCRIPTION

- Hypocalcemia is defined as a corrected total serum calcium level < 8.5 mg/dl (<2.12 mmol/l) or ionized serum calcium level <4.5 (<1.13mmol/l)
- Total calcium should always be corrected for serum albumin. Corrected calcium = measured calcium + [0.8 x (4.0- serum albumin)]
- Hypocalcemia is a common problem in clinical practice, both in ambulatory care and in hospitalized patients. More than 80% critically ill patients develop hypocalcemia.
- The major factors that influence serum calcium concentration are parathyroid hormone (PTH), vitamin D activity and their action on the kidneys and the intestine.
- Hypocalcemia is mainly caused by disorders related the level or activity of parathyroid hormone and/or vitamin D.
- The clinical presentation of hypocalcemia could vary from asymptomatic (incidental finding) to a life threatening one depending on the rapidity of development and severity.

Major causes of hypocalcemia

1. **Hypocalcemia with inadequate PTH (low or inappropriately normal PTH)**
   - Surgical removal (commonly post thyroidectomy or parathyroidectomy)
   - Neck radiation
   - Autoimmune destruction
   - Idiopathic hyperparathyroidism
2. **Hypocalcemia with high PTH**
   - Chronic kidney disease
   - PTH resistance: pseudohypoparathyroidism
   - PTH resistance; hypomagnesemia
   - Vitamin D deficiency: Nutritional or malabsorption
   - Vitamin D resistant: Vitamin-D dependent or resistant rickets
3. **Miscellaneous**
   - "Hungry bone syndrome" following parathyroidectomy
   - Extravascular deposition of calcium: hyperphosphatemia, pancreatitis, tumor lysis syndrome
   - Critical illness
   - Drugs: IV bisphosphonate therapy

CLINICAL FEATURES

Symptoms and signs

- Chronic hypocalcemia is generally asymptomatic or cause mild symptoms.
- The hallmark of hypocalcemia is an irritable neuromuscular system which shows spontaneous or induced hyperexcitability, called tetany.

- Mild symptoms: perioral numbness, paresthesia of the hands and feet, muscle cramps, fatigue
- Severe clinical manifestations

1. **Tetany:**
    - o Spams of hands and/or feet (carpopedal spasm): forced inward movement (adduction) of the thumb, flexion of metatarsophalangeal joints and wrists
    - o Laryngeal spams: stridor or change in voice, air hunger
    - o Induced tetany
        - **Trousseau's sign:** Carpal spasm induced but inflating sphygmomanometer 20mmHg above the systolic BP and keeping it for 3 minutes.
        - **Chvostek's sign**: elicited by tapping the facial nerve about 2cm in front of the ear (tragus) and observing contraction of the facial muscles. Chvostek's sign can also be seen in normal individuals. It has poor sensitivity and specificity.
2. **CNS manifestations**: Focal or generalized seizures, confusion, delirium, papilledema
3. **Cardiac manifestations:** hypotension, features of heart failure, prolonged QT on ECG
4. **GI manifestations**; abdominal cramps, biliary colic

- Clinical features related to the underlying disease
    - o Chronic hypoparathyroidism:
    - o cataracts, poor dentition, dry skin, brittle nails, coarse hair, basal ganglia calcifications
    - o Vitamin D deficiency in adults: diffuse bone pain and muscle weakness

INVESTIGATIONS AND DIAGNOSIS

- ECG: look for prolonged QT interval

- If the cause of hypocalcemia is obvious e.g., post-thyroidectomy or post-parathyroidectomy, advanced chronic disease, or tumor lysis, further investigation might not be needed.
- The most important investigations need for identifying the possible cause of hypocalcemia are the following
  - Creatinine and BUN
  - Serum magnesium and phosphorus
  - Serum PTH (preferably intact PTH)
  - vitamin D level (25(OH)vitamin D)

TREATMENT

OBJECTIVES OF TREATMENT

- Prevent and correct life-threatening complications

Non-pharmacologic

- Increase diet rich in calcium and vitamin D.

Pharmacologic

1. **Hypocalcemia with severe symptoms** (tetany, seizure, change in mental status, prolonged QT) or acute(postoperative) <7.5mg/dl: IV calcium
   - **Calcium gluconate (10%) 01 ampoule (10ml**) IV over at least 10min (rule of 10)
   - If symptoms persist, repeat the above. Don’t repeat more than two times.
   - Give a continuous infusion(drip) of calcium in the following way
     - Add 06 ampoules of 10% calcium gluconate in1liter of 5%DW run 12 hourly (80ml/hr or 28drops/minute).
     - This equivalent to 540mg of elemental calcium in 1000ml = 0.54mg/ml preparation running at about 45mg/hour)

- Do serum calcium every 12 hour and continue infusion until calcium reaches 8mg/dl
- Start oral calcium (see below) as soon as the patient is able to take orally, overlap with the intravenous infusion.

2. **Severe hypocalcemia in the presence of hypomagnesemia**: correct the magnesium first
   - IV magnesium sulfate: see hypomagnesemia treatment in standard treatment guideline.
   - Give also calcium gluconate as above.
3. **Long-term calcium replacement therapy**: for mild hypocalcemia and after IV calcium in sever hypocalcemia.
   - Give elemental calcium 1500 to 2000mg/day in two to three divided doses
     - **Calcium carbonate 1000mg** (equivalent to 400mg elemental calcium), 2tabs, PO, 8-12hourly
   - Target serum calcium is to keep it between 8-9mg/dl. Don't go beyond 9mg/dl.
4. **Vitamin D supplementation or correction of deficiency** (if confirmed) …see on vitamin D deficiency in adults
   - Vitamin D3 or D2: If deficiency confirmed (50,000IU weekly for 6-8weeks), if not yet confirmed, give 800IU/day empirically.

REFERRAL

- Patients with hypocalcemia, the etiology of which is not clear or can't be investigated in the setting should be referred.

FURTHER READING

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2. Jeremy Fong, Aliya Khan. Hypocalcemia. Updates in diagnosis and management for primary care. Can Fam Physician 2012; 58:158-62.

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9.3.4 MAGNESIUM DISORDERS

9.3.4.1 HYPOMAGNESEMIA

BRIEF DESCRIPTION

- Magnesium is the second most abundant intracellular cation in the body.
- It is predominately stored in bones followed by the intracellular compartment of muscles and soft tissues
- The kidney is the major organ responsible for regulating serum magnesium.
- Magnesium plays key role in variety of cellular processes. It is required in all enzymatic reactions requiring adenosine triphosphate (ATP), neuromuscular excitability and cell permeability, regulation of ion channels, cellular proliferation and apoptosis.
- The major dietary sources of magnesium are green vegetables (such as spinach), nuts and whole grains (cereals). About 30-40% of the dietary magnesium is absorbed in the GI, mainly small intestine
- Units of serum magnesium measurement and normal values:
  - Serum magnesium can be reported in any of the three units: mmol/l, mEq/l or mg/dl.
  - The molecular weight of magnesium is **24.3** and its valence is 2 (+2). Hence. the relationship between the units is as follows

1. mEq/l = mmol/L x 2 OR mmol/l= mEq/l ÷ 2

2. mg/dl = 2.43 x mmol/l OR mg/dl= 1.21 x mEq/l

- The normal range for serum magnesium is 1.7 to 2.1 mg/dl= 1.4 to 1.7 mEq/l= 0.70 to 0.85 mmol/L.

- Hypomagnesemia is defined as serum magnesium <1.6mg/dl or < 0.66 mmol/L (<1.3mEq/L). Clinically significant symptoms and signs do not commonly occur until the level falls below 1.2 mg/dL.
- Hypomagnesemia is common in hospitalized patients, particularly critically ill patients.
- The mechanisms of hypomagnesemia development are renal losses, GI losses or poor intake, redistribution (shift or sequestration) or a combination. See the table below for common causes of hypomagnesemia. (See the table below)

Table 9.3. Causes of hypomagnesemia

Mechanisms	**Causes**
A. Renal loss	1. Medications • Loop or thiazide diuretics (Not potassium sparing diuretics) • Nephrotoxic medications: aminoglycosides, amphotericin B, Cisplatin and Cyclosporine 2. Polyuric states • Postobstructive diuresis • Polyuric phase of recovering AKI(ATN) • Diabetic ketoacidosis (DKA) 3. Extracellular fluid expansion (hyperfiltration) • Aggressive saline infusion 4. Hypercalcemia 5. Inherited renal tubular disorders: Gitelman or Barrter syndrome

B. Gastrointestinal causes	1. Diarrhea 2. Prolonged NG tube suction or prolonged vomiting 3. Prolonged PPI use 4. Malabsorption 5. Small bowel resection 6. Severe malnutrition 7. Chronic alcohol dependence
C. Redistribution (shifting in to the intracellular space) **or** **sequestration**	1. Correction of Diabetic ketoacidosis (DKA) 2. Refeeding syndrome 3. Hungry bone syndrome: after parathyroidectomy or thyroidectomy 4. Acute pancreatitis

Clinical features

Symptoms and signs

- **Asymptotic**: Mild (1.2 -1.6mg/dL) hypomagnesemia developing slowly is usually asymptomatic.
- **Symptomatic:** The major manifestations are neuromuscular, cardiovascular, and refractory electrolyte abnormalities.
    - **Neuromuscular: Neuromuscular hyperexcitability**
        - Positive Chvostek's and Trousseau's signs
        - Tetany

    - Tremor, fasciculation
    - Seizure
    - Confusion
  - **Cardiovascular: ECG abnormalities or life-threatening ventricular arrhythmias**
    - Early ECG abnormalities: Wide QRS, peaked T-wave
    - Late ECG abnormalities: Progressive widening of QRS, prolonged PR interval and diminished T-wave
    - Arrhythmias: Torsades de pointes, a repetitive polymorphic ventricular tachycardia with QT prolongation
    - Increase risk of digoxin toxicity
  - **Electrolyte abnormalities**
    - Hypokalemia: refractory to potassium replacement alone
    - Hypocalcemia: refractory to calcium and vitamin D treatment alone
  - **Normal serum magnesium with magnesium depletion**
    - Patients with refractory hypokalemia and hypocalcemia should be suspected to have magnesium depletion despite normal serum magnesium. This is particularly true for patients with risk factors (e.g., chronic diarrhea, alcohol abuse, long term diuretic use)

DIAGNOSIS AND INVESTIGATION

Diagnosis

- **Whom to screen for hypomagnesemia?**
  - Critically ill patients admitted to ICU
  - All patients with hypokalemia or hypocalcemia
  - Patients with clinical manifestations suspicious of hypomagnesemia

  - Patients with potential causes for hypomagnesemia: chronic diuretic use, nephrotoxic medication, prolonged PPI use, polyuric patients, chronic diarrhea, alcohol dependence, post parathyroidectomy/thyroidectomy

- **Confirming hypomagnesemia:**
  - serum magnesium level (watch the unit)
- **Identifying the cause of hypomagnesemia**
  - A careful history often provides enough information to identify the cause: drug history, history of diarrhea, alcohol use, and nutritional assessment.
  - If the cause is not obvious determine 24hour urine magnesium. A 24hour urine magnesium excretion >10mg should be considered renal wasting and <10mg suggests GI loss or transcellular shift.

INVESTIGATION: ADDITIONAL INVESTIGATIONS NEEDED

- Serum potassium
- Serum calcium
- ECG
- Serum creatinine: To help decide the rate of treatment

TREATMENT

Non-pharmacologic treatment

- **Correction of the underlying cause**: e.g., discontinuation of diuretics, nephrotoxic medications, treating diarrhea, helping to decrease/quit alcohol.
- **Increase dietary intake of magnesium**: Food rich in magnesium: Green leafy vegetables, nuts or peanuts, legumes, (e.g., beans), soy milk, and whole grains

PHARMACOLOGIC TREATMENT

I. Treatment of severe (<1.2mg/dl) and symptomatic hypomagnesemia

- **Life threatening** (arrhythmia)
  - **IV Magnesium sulfate** 1- 2g, IV push over 3-5 minutes.
  - Followed by continuous infusion
- **Emergent**: No arrhythmia but severe symptoms (e.g., neuromuscular manifestations)
  - **IV Magnesium sulfate, 1 to 2g diluted in 100mL D5W**, run 15-30minutes.
  - Followed by continuous infusion.
- **Non-emergent repletion** in patients with severe hypomagnesemia
  - Start with continuous infusion. Avoid the initial bolus.
- **How to give continuous infusion?**
  - 4 -6 g magnesium sulfate diluted in 1-2 liters of D5W to run over 12 to 24 hours. E.g., 3g magnesium sulfate in 1000ml D5W runs 12 hourly.
- **Duration of continuous infusion**
  - Continuous infusion should continue for **two more additional days** after correction of the serum magnesium.
- **Patients with significantly impaired kidney function (eGFR<30ml/min):**
  - Because of the risk for severe hypermagnesemia, 50% of the magnesium sulfate dose described above should be given.
- **Monitoring serum magnesium**
  - Serum magnesium should be determined 1-2 times per day
- **Major adverse effect**
  - The major adverse effect of IV magnesium sulfate is iatrogenic hypermagnesemia, which almost exclusively occurs in patients with impaired kidney function.

  - Monitor for depressed/absent deep tendon refluxes, bradycardia and low BP, which are the major the major manifestations of hypermagnesemia.

II. Moderate hypomagnesemia (1.2- 1.5mg/dl) in inpatient setting

- **IV** magnesium sulfate 2gm in 1000ml D5W to run 12-24 hours.

III. Continue Potassium or Calcium infusions

- In patients with severe hypokalemia or hypocalcemia associated with hypomagnesemia, **IV infusions of potassium or calcium should be continued** as correction of magnesium takes long periods of time (a few to several days)

IV. Oral magnesium

- Oral magnesium should be started along with or after IV magnesium sulfate.
- Most oral magnesium preparations are poorly absorbed and poorly tolerated (due to diarrhea)
- 240 -1000mg of elemental magnesium is needed in 24 hours.
- The most commonly available oral magnesium preparation available is magnesium hydroxide.
  - **Magnesium hydroxide (liquid form),** 400mg/5ml (168mg elemental Mg5ml) give 10ml BID-TID.
  - If it is combined with Aluminum, avoid prolonged use.

V. Pharmacologic treatment of renal potassium loss (wastage):

Potassium sparing diuretics also spare magnesium.

- In situations where is continued renal loss of magnesium, give magnesium alone fails to correct the hypomagnesemia.
- These situations include: continued need to use diuretics, nephrotoxic medications until tubular injury recovers (Cisplatin, Amphotericin B, Aminoglycosides), inherited tubulopathies (Gitelman or Barrter syndrome).

- **Spironolactone** starting dose 25-50mg/day or 2 divided doses, maximum 400mg/day or in two divided doses

REFERRAL

- If hypomagnesemia is refractory, recurrent or the cause is not clearly identified, the patient should be referred to the next higher tier.

FURTHER READING

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2. Mohammad Tinawi. Disorders of Magnesium Metabolism: Hypomagnesemia and Hypermagnesemia. Arch Clin Biomed Res 2020; 4 (3): 205-220.
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9.3.4.2 HYPERMAGNESEMIA

BRIEF DESCRIPTION

- Hypermagnesemia is defined as a serum magnesium level **> 2.5mg/dL** (>1.1mmo/L or > 2.2mEq/L). However clinical symptoms do not generally occur unless serum magnesium is **>5mg/dL**.
- Hypermagnesemia is relatively uncommon in clinical practice and symptomatic hypomagnesemia is much less common. This is due to the kidney's tremendous capacity to excrete excess body magnesium.
- Hypermagnesemia occurs in three clinical settings
    - **Marked impairment in kidney function** (acute or chronic)
    - **Iatrogenic or accidental excess infusion or ingestion** of magnesium: typically, in the setting of treatment for preeclampsia or eclampsia with IV magnesium sulfate
    - **Excess release from the intracellular compartment** (generally with impaired kidney function): Tumor lysis syndrome, rhabdomyolysis.

CLINICAL FEATURES

Symptoms and signs

- **Asymptomatic**: serum magnesium level **2.5-5mg/dL**, though defined as hypermagnesemia, is generally asymptomatic unless there is a concomitant hypocalcemia.
- **Symptomatic**: The major symptoms and signs of hypermagnesemia are related to neuromuscular or cardiovascular system.
    - o **Neuromuscular:** characterized by depressed neuromuscular conduction(activity)
        - – **Mild:** Nausea, vomiting, constipation, facial flushing, dizziness, depressed deep tendon reflexes.
        - – **Moderate:** Absent deep tendon reflexes, drowsiness, paralytic ileus, urinary retention, blurred vision, and hypotension.
        - – **Severe (life threatening):** flaccid paralysis, respiratory depression, coma, apnea.
    - o **Cardiovascular**: characterized by delayed(depressed) cardiac conduction
        - – **ECG abnormalities (every conduction is delayed):** prolonged PR interval, AV block, prolonged QRS duration, prolonged QT interval.
        - – **Severe (Life threatening):** bradycardia advanced AV-block, cardiac arrest/asystole.
    - o **Hypocalcemia:** hypermagnesemia suppresses PTH secretion

Table 9.4. Correlation between serum magnesium level and clinical manifestations

Serum magnesium level	Symptoms/signs
5-7mg/dl	○ Nausea, vomiting, constipation ○ Facial flushing ○ Dizziness
7-12mg/dl	○ Urinary retention, ileus, ○ Blurred vision, confusion, lethargy ○ Loss of deep tendon reflexes ○ Prolonged PR interval, wide QRS, prolonged QT ○ Hypotension
>12mg/dl	○ Flaccid paralysis ○ Respiratory depression ○ Coma ○ Advanced AV-block/bradycardia ○ Cardiac arrest

Adapted from: Arch Clin Biomed Res 2020; 4 (3): 205-220 (Reference #3)

DIAGNOSIS AND INVESTIGATIONS

- A serum magnesium level >2.5mg/dl confirms the presence of hypermagnesemia.
- Additional important investigations needed in those with confirmed hypermagnesemia

  - Renal function test: creatinine and eGFR
  - Serum calcium, phosphorous and potassium
  - ECG
- **Monitoring serum magnesium level**: patients receiving parenteral magnesium sulfate need baseline renal function test, ECG, close follow up of serum magnesium, deep tendon reflexes and mental status.
- **Additional history**: history of excess magnesium ingestion (antiacids or magnesium-based laxatives).

TREATMENT

NON-PHARMACOLOGIC

- Stop magnesium infusion or oral magnesium containing drugs.
- Hemodialysis: In symptomatic hypermagnesemia with impaired kidney function

PHARMACOLOGIC

- **Symptomatic hypermagnesemia:**
  - **Intravenous calcium**
    - **Calcium gluconate 10%,** 10ml, diluted in 100ml D5W to run over 5-10 minutes.
    - In patients with cardiac arrest, give undiluted over 2-3 minutes.
    - Repeat the dose, if symptoms persist.
  - **Forced diuresis**
    - **Normal saline 200ml/hour** for 6 -12 hours, if the patient does not have volume overload (edema, pulmonary congestion, and hepatomegaly).
    - Give **Furosemide 40mg, IV, stat**, in the middle of the NS infusion.
  - **Hemodialysis**

      - In patients with significantly impaired kidney function (eGFR<30ml/min) and symptomatic hypermagnesemia, excretion of the magnesium is unlikely to happen; hence urgent hemodialysis is needed after giving.

- **Asymptomatic hypermagnesemia**
   - No need for pharmacologic treatment.
   - Stopping magnesium containing medications or magnesium sulfate infusion, if being given, will suffice.

PREVENTION

- During parenteral magnesium sulfate administration
   - Determine baseline serum creatinine and continuously monitor urine output
   - Monitor serum magnesium regularly every 6 hours
   - If possible, have ECG monitoring (bedside monitor)
- Avoid prolonged use of magnesium containing medications in patients with impaired kidney function medications (antacids or magnesium containing laxatives)

REFERRAL

- Patients with symptomatic hypermagnesemia and impaired kidney function need to be referred for hemodialysis after stabilization with calcium gluconate (see above).

FURTHER READING

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9.4 GLOMERULAR DISEASES

9.4.1 NEPHRITIC SYNDROME: ACUTE GLOMERULONEPHRITIS (AGN) AND RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN)

BRIEF DESCRIPTION

- **Acute glomerulonephritis (AGN) and rapidly progressive glomerulonephritis (RPGN)** are important causes of acute kidney injury. in that they have clearly identifiable clinical features and can rapidly progress to end stage renal disease.
- AGN and RPGN present more or less in a similar fashion. Their presentation is commonly described as the **nephritic syndrome**.
- The clinical difference between AGN and RPGN: It is not easy to clinically differentiate between the two.
    - In RPGN: The kidney function keeps of deteriorating over days to weeks, unless treated. It progresses to end stage renal disease unless treated early.
    - In infection related AGN: The kidney function usually improves.
- The most common causes of self-limiting AGN are bacterial infections (also called infection related glomerulonephritis).
- As opposed to pediatric AGN, where the commonest cause is streptococcal infection of the skin or the throat, adult AGN can occur following any bacterial infection at any site.
- The most important causes of RPGN are autoimmune diseases: SLE (systemic lupus erythematosus), systemic small vessel vasculitis (ANCA-vasculitis), antibody direct to glomerular basement membrane (Anti-GBM disease).
- The histopathologic finding in both AGN and RPGN is described as diffuse proliferative glomerulonephritis and crescentic glomerulonephritis respectively.

CLINICAL FEATURES

Symptoms and signs

- **Clinical features of the AGN/RPGN: the nephritic syndrome**
    - Acute onset body swelling (Edema) and shortness of breath
    - Decreased urine amount (oliguria)
    - Reddish urinary discoloration (typically tea or cola colored urine)
    - High blood pressure
- **Clinical features of suggesting the underlying causes (systemic diseases)**
    - Hair loss/diffuse non-scaring alopecia – SLE
    - Malar rash, photosensitive rash, non-pruritic rash over the body– SLE
    - Joint pain, evidence of arthritis (swelling and tenderness of joints) – SLE
    - Hemoptysis, cough and dyspnea – Vasculitis, Anti-GBM disease or pulmonary edema
    - Petechiae/purpura – Vasculitis or SLE
    - Pleural effusion – Part of the complication or SLE associated
    - Pericarditis (friction rub or distant heart sound) – SLE or uremic pericarditis
    - Cardiac murmurs – Infective endocarditis or SLE
    - Focal neurologic deficit – SLE (Lupus cerebritis) or vasculitis
- **Clinical features related to marked decrement in the kidney function**
    - Pulmonary crackles – pulmonary congestion
    - Nausea and vomiting – uremic gastropathy
    - Change in mental status – uremic or hypertensive encephalopathy

- Mucocutaneous bleeding – uremic bleeding

DIAGNOSIS AND INVESTIGATIONS

Diagnosis

- The diagnosis of AGN or RPGN should be made clinically in any patient presenting with the nephritic syndrome (acute onset body swelling, tea/cola colored urine, oliguria, and high BP)
- Further investigations are needed for three purposes: For confirming the nephritic syndrome, for identifying possible etiologies, and complications.

INVESTIGATIONS

- **Investigation for evidencing the presence of the nephritic syndrome (AGN/RPGN)**
    - **Urinalysis:**
        - Hematuria and proteinuria
        - The RBCs in the urinalysis: Significant proportion are dysmorphic
        - RBC casts: may or may not be present. Their presence is not mandatory for diagnosis)
    - **24hour urine protein:** above 500mg (usually>1000mg), it can sometimes be nephrotic range(>3000mg)
    - **Serum creatinine and urea**
- **Investigations for assessing potential complications**
    - **Serum electrolytes:** particularly serum potassium (to look for hyperkalemia).
    - **Chest X-ray:** for evidence of pulmonary edema or pleural effusion.
- **Investigations for identifying possible etiology**
    - **Basic serologies: to be done at initial evaluation**
        1. **Anti-streptolysin titer (ASO)**: For preceding streptococcal infection

  - It may be falsely low or negative in patients with skin infections.
  - It remains a useful test in those with pharyngitis but antibiotics may decrease the titer

2. **The streptozyme test**
  - It is a much better than ASO alone (has high sensitivity and specificity) for checking a preceding streptococcal infection.
  - Hepatitis B (HBV) and C (HCV) serology: HBSAg and HCV antibody.
  - HIV screening
  - ANA (anti-nuclear antibody)

- **Additional important diagnostic investigations**: to ordered by specialist who would decide on definitive management
  - Anti-double strand DNA antibody(anti-dsDNA)
  - Anti-neutrophil cytoplasmic antibody test (ANCA)
  - Anti-glomerular basement antibody (Anti-GBM antibody)
  - Serum complement level (complement -3 and 4/C3 and C4 levels)
  - Renal biopsy
- **Investigation for looking evidence of chronicity**
  - **Abdominal ultrasound:** bilateral small kidneys in adults (<9cm longitudinally) indicate chronic kidney disease. Normal or increased kidney size can be found in both acute and chronic glomerular diseases.

TREATMENT

Non-pharmacologic treatment

- Salt and fluid restrictions
- Dialysis: if there are indications (see the topic acute kidney injury for indications)

PHARMACOLOGIC TREATMENT

Supportive (symptomatic) management

- **Loop diuretics**
  - **Oral Furosemide:**
    - For patients with mild peripheral edema.
    - Starting dose 40mg PO BID.
    - Follow every 2-3 days, increase the dose to higher dose (Maximum dose 600mg/day) or admit for IV diuresis, if response is suboptimal or there is worsening.
  - **IV Furosemide:**
    - For patients with pulmonary congestion or sever edematous state
    - Start with 40mg IV, stat. See response every 2 hours. If urine output of 150ml and above is achieved in 2 hours and give the 40mg IV BID or TID.
    - If urine output is <150ml in 2hours, increase the dose by 40mg and reassess the urine output in another 2 hours.
    - Give the dose which resulted in adequate once diuresis (>150ml/2hour) as standing e.g. 80mg or 120 IV BID or TID. Maximum bolus dose 200mg.
    - IV Furosemide above 100mg should be given slowly (over 15-20minutes)
  - **Avoid prophylactic potassium tablet or spironolactone:** due to the risk of hyperkalemia in patients with AGN/RPGN.
- **Antihypertensives**

- ○ **Loop diuretics** are the preferred Antihypertensives**:** see above on diuretic
- ○ **Additional Antihypertensive:** If BP is not well controlled with loop diuretics alone
    - – **Add Calcium channel blocker on loopr diuretics:**
        - ✓ **Amlodpine** 5-10mg PO once daily

        OR

        - ✓ **Nifedipine** 20-40mg PO BID.
    - – **If a third agent is needed** (on top of Furosemide and Calcium channel blocker combination) add a beta-blocker**:Alterantaives**
        - ✓ **Carvedilol** 6.25 to 25mg BID
        - ✓ **Bisoprolol** 2.5 to10mg/day or
        - ✓ **Metoprolol** 25-100mg/day or
        - ✓ **Atenolol** 25-100mg/day
    - – **Avoid ACE inhibitors, Angiotensin receptor blockers (ARBS):** due to the risk of hyperkalemia and potential for deterioration in kidney function.
    - – **Avoid Spironolactone** in patients with AGN/RPGN: due to risk of hyperkalemia and worsening kidney function.

- **Management of hyperkalemia**
    - ○ Start shifting treatment with regular insulin < if serum potassium is >6.0mmol/l
        - – **Regular Insulin:** 10IU regular insulin IV, immediately followed by 03vials (60ml) of 40% dextrose IV, to be given every 6 hours. Monitor blood sugar every 4-6 hourly.
    - ○ If potassium is >7mmol/l or there are ECG changes hyperkalemia start IV calcium

- **Calcium gluconate (10%) 10ml,** IV, to be given over 5 minutes followed by regular insulin (as above).

DEFINITIVE MANAGEMENT OF THE UNDERLYING CAUSE

- Definitive management of the underlying cause might require early initiation of intensive immunosuppressive therapy; hence, patients should be referred to nephrologist as soon as possible.

REFERRAL

- All patients with nephritic clinical presentation should be referred to a hospital where there is a nephrology service.

FURTHER READING

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_9.4.2 NEPHROTIC SYNDROME (NS) IN ADULTS

BRIEF DESCRIPTION

- Nephrotic syndrome (NS) is a clinical sate which results from heavy (massive) proteinuria.

- The presence of nephrotic syndrome (NS) is a definitive indicator of glomerular pathology.

- Nephrotic syndrome is defined if all the following three clinical and laboratory findings are fulfilled

  - **Heavy proteinuria**: defined as urine protein >3000mg(3gm) in a 24hr urine protein
  - **Hypoalbuminemia:** Defined as serum albumin <3g/dl
  - **Edema (edematous state)**
  - **Hyperlipidemia**, usually severe, is a common finding. Some experts include it as requirement for the diagnosis of NS.

- Some patients might have heavy proteinuria (>3000mg in 24-hour urine) but do not have the other features of the NS. They are said to have nephrotic range proteinuria, but not the nephrotic syndrome.
- Increased susceptibility to infection, venous thrombosis, and acute kidney injury are the major complications of the NS.
- Nephrotic syndrome is not a single disease. It is a manifestation of several diseases. Hence, once the presence of NS is confirmed, the etiology should be identified.
- Nephrotic syndrome in adults is different from pediatric NS in etiology, the needed investigation, treatment, and outcome. Hence, **adult NS should never be treated like pediatric NS.**
- The causes of nephrotic syndrome are classified in to two major groups: Primary (diseases limited to the glomeruli) and secondary (systemic diseases with glomerular manifestations or complications)
- Diabetes (diabetic kidney disease) is the leading cause of nephrotic range proteinuria worldwide.

Table 9.5. Major causes of nephrotic syndrome in adults

A. **Major cause of primary nephrotic syndrome**	B. **Major causes of secondary nephrotic syndrome**
I. Primary Focal segmental glomerulosclerosis (FSGS)	I. Diabetes
II. Minimal change disease (MCD)	II. Autoimmune disease: SLE
III. Primary membranous nephropathy (MN)	III. Infectious: HBV, HCV, HIV, Syphilis, Schistosomiasis
IV. Primary membranoproliferative glomerulonephritis (MPGN)	IV. Amyloidosis: primary or secondary amyloidosis
	V. Drugs: NSAIDS
	VI. Preeclampsia
	VII. Malignancy: Multiple myeloma, lymphoma, carcinomas

CLINICAL FEATURES

Symptoms and signs

- **Symptoms and signs related to the nephrotic state**
    - **Body swelling:** Periorbital edema, peripheral edema, scrotal or labial edema
    - **Third space fluid collection:** ascites, pleural effusion
    - **Fatigue and shortness of breath**
    - **Urine:** excessive foaming
    - **Nail:** white horizontal bands on the nail
- **Clinical features suggestive of specific secondary causes**
    - **Diabetes:** Known history of diabetes, presence of diabetic retinopathy

- **SLE:** diffuse non-scarring hair loss, malar rash, photosensitivity, polyarthritis
- **Preeclampsia:** third trimester pregnancy or peripartal state with high BP
- **Multiple myeloma:** bone pain, pathological fracture, anemia
- **Lymphoma:** Lymphadenopathy, splenomegaly
- **Carcinomas:** Local symptoms (breast lump, abdominal mass, cough/ hemoptysis, lymphadenopathy)

DIAGNOSIS AND INVESTIGATION

Diagnosis

- The following steps are helpful in guiding the diagnosis nephrotic syndrome in adults

Step 1: Confirming the presence of nephrotic syndrome:

- 24-hour urine protein
- Serum albumin
- Lipid profile

Step 2: Investigation for common causes of nephrotic syndrome

- **Retinal screening** for diabetic retinopathy: any time for type 2 diabetics and after a minimum of five year of type 1 diabetes
- **HBSAg, HCV antibody, HIV screening, VDRL(RPR), ANA**
- **AntiPLA2R antibody**: For screening primary membranous nephropathy
- **Work up for multiple myeloma:** If suspected, serum free light chains and serum electrophoresis.
- **Work up for other malignancies**: only if there are clinical clues.

Step 3: Renal biopsy

  - Unlike pediatric patients almost all non-diabetic adult patients with nephrotic syndrome need renal biopsy to confirm the etiology. Hence, they need to be referred to a hospital with nephrology service.

- **Investigations**: **Additional helpful investigations**
  - Urinalysis**:** hematuria and proteinuria
  - **Renal function tests (serum creatinine):** AKI can occur as a complication of the NS or over-diuresis or could be part the glomerular disease (nephrotic-nephritic presentation)
  - **Serum electrolytes:** As baseline for diuretic therapy
  - **Abdominal ultrasound**: to see kidney sizes
  - **Investigations when complications are suspected**: e.g., if deep vein thrombosis (a common complication is suspected), do doppler ultrasound of suspected limb veins.

TREATMENT

Non-pharmacologic treatment

- Salt restriction
- Fluid restriction (less than 1 - 1.5 liter/day)
- Encourage ambulation
- Protein should not be restricted rather encourage patients to take adequate protein and high calorie diet

PHARMACOLOGIC TREATMENT

1. Treatment of the edematous state

- **Loop diuretics:** nephrotic syndrome is associated with relative diuretic resistance
  - **Oral Furosemide:**
    - Starting dose 40mg, PO, BID -TID.
    - Increase the dose to 80 mg PO BID-TID, then 120mg. PO, BID-TID.

- **Aim**: decrease weight by 0.5 to 1kg/day.
- **IV Furosemide:** If no adequate weight loss with increasing dose, admit for IV Furosemide
  - Start with 40mg, IV, TID.
  - Increase the dose to 80 mg IV TID, then 120mg. PO, TID
  - If no adequate response with IV Furosemide, add **hydrochlorothiazide 12.5 to 25mg BID** (to be given 30 minutes before the IV Furosemide)
- Add prophylactic **KCl tablets (600mg BID-TID) or Spironolactone 25-50mg** PO/daily and monitor serum electrolytes every 2-3days.

2. **Anti-proteinuric treatment**

- **ACE inhibitors or Angiotensin receptor blockers (ARBS)**
  - Start after adequate diuresis.
  - The kidney function must be stable before starting.
  - The dose should be escalated gradually with monitoring of serum creatinine and potassium. Monitoring should be done within 2 weeks of initiation and dose escalation.
  - ACE inhibitors (particularly Enalapril) are preferred over ARBs due to their low cost and wide availability.
    - **Preferred**
      - ✓ **Enalapril:** starting dose 5mg BID, Maximum dose 20mg BID
    - **Alternatives**
      - ✓ **Lisinopril**: starting dose 5mg/day, Maximum dose 40mg/day
      - ✓ **Perindopril**: starting dose 5mg/day. Maximum dose 15mg/day

- ✓ **Telmisartan**: Starting dose: 40mg/day maximum dose 80mg/day
- ✓ **Irbesartan**: Starting dose: 75-150mg/day, maximum dose 300mg/day
- ✓ **Losartan**: Starting dose 50mg/day maximum dose 100mg/day
- ✓ **Valsartan**: Starting dose 80 -160mg/day, maximum dose 320mg/day
- ✓ **Candesartan**: Starting dose 8-16mg/day maximum dose 32mg/day

3. Pharmacologic treatment for complications of the nephrotic syndrome

- **Treatment of hyperlipidemia**: as per dyslipidemia treatment guideline (see section on dyslipidemia). Many patients require statins due to sever hyperlipidemia.
- **Prophylactic anticoagulation**: Indicated if serum albumin is <2g/dl and patient is hospitalized
  - ○ **Unfractionated heparin 5,000IU, BID** until discharge

    Or
  - ○ **Enoxaparin 40mg, SC, daily** until discharge
- **Therapeutic (Full dose) anticoagulation: Indications**
  - ○ If there is active venous thromboembolic disease (e.g. DVT/PE, renal vein thrombosis)
  - ○ If their albumin is low and the following risk factors are found: Pregnancy, active malignancy, recent major surgery, NYHA class III or IV heart failure or morbid obesity
    - – **Unfractionated heparin 17,500 SC, BID or Enoxaparin 1mg/kg/dose BID + Warfarin** (dose to be adjusted according to INR)

  - **Overlap heparin with warfarin** until two therapeutic INRs (2-3) achieved, and then followed by Warfarin alone.
  - **Duration of anticoagulation**: Until the nephrotic syndrome resolves or 6-12 months (if it does not resolve).

4. **Treatment of the specific cause of the nephrotic syndrome**

- **Empiric steroid or any immunosuppressive should not be started** for adults with nephrotic syndrome without doing renal biopsy; hence, all adult patients with non-diabetic nephrotic should be referred to a hospital with nephrology service.

REFERRAL

- All adult patients with non-diabetic nephrotic syndrome should be referred.

FURTHER READING

1. Charles Kodner. Diagnosis and Management of Nephrotic Syndrome in Adults. Am Fam Physician. 2016; 93(6):479-485.
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9.5 BENIGN PROSTATIC HYPERPLASIA (BPH)

BRIEF DESCRIPTION

- Benign prostatic hyperplasia (BPH) refers to histologic entity characterized by proliferation of smooth muscle and epithelial cells of the prostate.
- Although BPH is a histologic description, the term is commonly used in clinical practice.
- Benign prostatic enlargement (BPE) a similar term used to describe a

clinically detectable enlargement of the prostate.

- BPH is a common problem among older men and results in a significant impairment in quality of life.
- The prevalence of BPH greatly increases with age. About 50% of men by age 50 years and 80% of men by age 80 years will have BPH.
- The enlarged prostate contributes to the development and progression of lower urinary tract symptoms abbreviated as LUTS via following two mechanisms.
    - **Static component**: bladder outlet obstruction (BOO) caused directly by the enlarged tissue.
    - **Dynamic component**: resulting from increased smooth muscle tone and resistance within the enlarged prostate.
- In addition to LUTS, BPH can result in acute urinary retention, renal insufficiency, recurrent urinary tract infections or formation of bladder stone.
- BPH does not generally increase the risk of prostate cancer.

CLINICAL MANIFESTATIONS

Symptoms

- **Asymptomatic:** Not all men with enlarged prostate have symptoms. The correlation between presence and severity of symptoms does not correlate with the size the prostate.
- **Symptomatic:** the symptoms of BPH are classified in to two major groups. The severity of symptoms is variable but tends to be progressive.

1. **Storage symptoms**:
    - Day time increased urinary frequency
    - Nocturia
    - Urgency with or without urge incontinence.
2. **Voiding symptoms (symptoms during actual urination)**

  - Slow(weak) urine stream
  - Splitting or spraying of the stream
  - Intermittent urine stream
  - Straining
  - Hesitancy
  - Terminal dribbling
- **Acute urinary retention (AUR):** is the most common urologic emergency seen in patients with BPH.
  - Abrupt onset inability to pass urine associated with suprapubic or lower abdominal discomfort/pain.
- **Chronic urinary retention**
  - Patients may not have chronic pain rather may have symptoms of overflow incontinence
- **Hematuria (microscopic or macroscopic)** can occur in patients with BPH. However, its presence should be taken simply due to BPH rather should prompt work up for other pathologies such as prostate or bladder cancer.
- **Symptom scores**: symptoms score, such as the international prostate symptom score (IPSS) are useful in evaluation the severity of symptoms, improvement with treatment, and impairment in quality of life.

SIGNS

- **Enlarged prostate:** The most important physical sign in the diagnosis of BPH is appreciation of diffusely enlarged, smooth surface, firm, non-tender prostate without nodules through digital rectal examination (DRE).
- **Full bladder:** patients with significant urinary retention might have enlarged (palpable) bladder on the suprapubic area.
- **Measurement of post-void urinary bladder volume:** the volume urine retained in the urinary bladder can be measured using **in-and-out catheterization.**

- Catheterization will be done immediately after the patients urinates; the volume of urine drained using the catheter will be documented.
- A post-void urine volume above 100ml is considered significant.

Table 9.6. International prostate symptom score (IPSS)

Patient Name: ______________________ ***Age*** ________ ***Date completed*** _______

No.	Questions? **In the last one month how often……**	Not at all	<1/ 5th of the time	Less than ½ of the time	About ½ of the time	>1/2 of the time	Almost always	Patient's score (Out of 5)
1	**Incomplete emptying** Have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2	**Frequency** Have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	

3	**Intermittency** Have you found, you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4	**Urgency** Have you found it difficult to postpone urination?	0	1	2	3	4	5	
5	**Weak stream** Have you had a weak urinary stream?	0	1	2	3	4	5	
6	**Straining** Have you had to push or strain to begin urination?	0	1	2	3	4	5	
7	**Nocturia** How many times, most typically, get up to urinate from the time you went to bed at night until the time you got up in the morning	0 (none)	1 (once)	2 (twice)	3 (3X)	4 4X)	5 (5 X or more)	

				Sum of scores			
	Total score: **0 to 7: Mild symptoms** **8 to 19: Moderate symptoms** **20 to 35: Severe symptoms**						
Quality of life due to symptoms	Delighted	Pleased	Mostly Satisfied	Mixed (equally satisfied & unsatisfied)	Mostly dissatisfied	unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6

DIAGNOSIS AND INVESTIGATION

Diagnosis

- The diagnosis of BPH is made based on clinical grounds: with the presence of storage or voiding symptoms along with finding of diffusely enlarged prostate on DRE.

Investigations

- **Ultrasound**
  - Abdominal (genitourinary) and prostate ultrasound
    - To estimate size(volume) the prostate: usually overestimates the size

    - –To evaluate for the presence of hydronephrosis and bladder stone
    - –For measurement of postvoid bladder volume
  - Transrectal ultrasound provides a better estimation of size; however, it should only be done when there is a plan to do surgical intervention.
- **Prostatic surface antigen (PSA)**
  - BPH is known to increase PSA. The size of the prostate correlates with the degree of PSA elevation.
  - Elevated PSA is not equivalent to diagnosis of prostatic cancer and a normal PSA does not exclude it.
  - Men with a total PSA >4ng/ml should be referred for urologic evaluation.
- **Urinalysis**
  - Urinalysis needs to be routinely at baseline and when there are indications e.g. suspicion of infection.
  - The presence of pyuria, bacteriuria, or nitrite in the urine does not mean that the patient should be prescribed antibiotics. Antibiotics are indicated if there are clear cut acute-onset irritative symptoms (dysuria and frequency) on top of the existing LUTS or if there are systemic symptoms such as fever.
- **Renal function test**
  - Serum creatinine and calculation of estimated GFR are needed at baseline and during follow up.

TREATMENT

NON-PHARMACOLOGIC

- **Watchful waiting**
  - Patients with mild symptoms (IPSS=0-7) and who are not bothered by their mild symptoms can be followed without any intervention.
- **Supportive treatment and patient education**

- Reassurance: The patient should be informed that BPH is not a cancer
- Lifestyle advice
  - –Reduce fluid intake: at night and when going out in public places
  - –Decreasing coffee and alcohol intake (due to their mild diuretic effects)
  - –Double voiding to empty the bladder more completely
  - –Voiding in sitting position than standing
  - –Timed-voiding schedule: Voiding at fixed time intervals
  - –Bladder retraining: encourage to hold urination when the patient has sensory to help him increase bladder capacity
  - –Decreasing dose and/or adjusting diuretics: Diuretics can worsen the symptoms and increase the risk of acute urinary retention. If possible, avoid or decrease or escape night dose of diuretic
  - –Treatment of constipation

- **Management of acute urinary retention (AUR)**
  - The mainstay of management of AUR is insertion of indwelling urinary catheter and keeping it for 1-2 weeks. Start alpha-1 blocker along with the catheterization (see below), remove the catheter after 1-2 and try voiding without catheter.
  - If retention recurs with the first trial, repeat catheterization and keep it for two more weeks and try to remove the catheter as above. If it fails for the second time, refer to urologist while the patient is catheterized.
- **Surgical management**
  - Surgical therapy (trans-urethral) should be offered as an option to all men with moderate or severe symptoms (IPSS>7).
  - Open prostatectomy is reserved for men with a very big prostate(>80ml) and have severe symptoms

PHARMACOLOGIC MANAGEMENT

- Patients with moderate (IPSS=8-19) or severe (>20) symptoms who are bothered by symptoms should be offered medical therapy.

First line

- **Alpha-1-blockers (alpha-1 adrenergic antagonists)**
    - **Alfuzosin** 10mg, PO, at bed time. No dose titration needed.

      OR

    - **Tamsulosin** 0.4mg, PO, at bed time. If symptoms don't improve in 4 weeks, the dose can be increased to a maximum of 0.8mg at bed time.
        - Side effects of these drugs can include orthostatic hypotension, headache, dizziness, nasal congestion, edema, fatigue and impaired sexual function.
        - Tamsulosin has shown a higher incidence of ejaculatory dysfunction.
        - They should be avoided if there is a recent plan for cataract surgery due to the associated floppy iris syndrome.

ALTERNATIVE

- **5-alpha reductase inhibitors (5-AR inhibitors)**
    - In patients who cannot tolerate alpha-1-blockers, do not have predominant irritative symptoms and do not have concomitant erectile dysfunction.
    - As they work by reducing the size of the prostate, they better work in men with larger prostate.
    - Patients should understand that treatment for 6 to 12 months is needed before prostate size is reduced and improvement in symptoms is seen.
        - **Finasteride 5mg, PO/day.** No dose titration needed

          OR

        - **Dutasteride 0.5mg, PO/ day.** No dose titration needed

  - The major side effects of these drugs are decreased libido and ejaculatory or erectile dysfunction. They should be avoided if there is a plan to conceive or if partner of the patient is pregnant.
  - 5-AR inhibitor reduce PSA level significantly, hence, PSA levels should be interpreted cautiously. A baseline PSA is needed.
- **Combination of alpha-1 blockers and 5-alpha reductase inhibitors**
  - Indications
    - Severe symptoms
    - Big size prostates with less satisfactory response to alpha-blockers alone.
    - **Tamsulosin (0.4mg) and Dutasteride (0.5mg) (Fixed dose combination)** one tablet at bed time.
    - The alpha-blocker might be discontinued after 6-9 months, if symptoms improve significantly

SECOND LINE

- **Long-acting** phosphodiesterase-5 inhibitors
  - In patients with mild to moderate symptoms (IPSS<20) symptoms, particularly if they have additional erectile dysfunction,
    - **Tadalafil 5mg, PO/ day.**
  - Combination of alpha-1-blocker with a phosphodiesterase-5 inhibitor should be avoided.

REFERRAL

- All men with preference or indication for surgical intervention need to be referred.

FURTHER READING

1. European Association of Urology Guidelines, 2017 edition.
2. J. Curtis Nickel, Lorne Aaron, Jack Barkin, Dean Elterman et al.Canadian Urological Association guideline on male lower urinary tract symptoms/

benign prostatic hyperplasia (MLUTS/BPH): 2018 update. *Can Urol Assoc J* 2018;12(10):303-12.

3. American Urological Association Guideline: Management of Benign Prostatic Hyperplasia (BPH), Revised 2010.

9.6 URINARY INCONTINENCE (UI)

BRIEF DESCRIPTION

- Urinary incontinence (UI) refers to involuntary leakage of urine. It is a very common but undertreated condition.
- Patients are generally reluctant to complain (discuss) about urinary incontinence due to embarrassment or lack of knowledge on the presence of treatment. Hence, physicians should proactively inquire about UI in high-risk individuals,
- UI affects many aspects of a patient's health. It can be associated with depression, anxiety, social isolation, sexual dysfunction, perineal infections (candidiasis, cellulitis) and increased care giver burden.
- Although old age is a major risk factor, urinary incontinence should not be considered as normal process of ageing.
- Urinary incontinence is classified in to five major groups: stress, urge, mixed, overflow and functional incontinence. The features of these groups is described in the table below(see clinical features below)
- The major risk factors for urinary incontinence are: old age, multiparity, menopausal vaginal atrophy, obesity, family history, neurologic diseases (Spinal cord diseases, Stroke, Parkinsonism), impaired functional status, diabetes, genitourinary surgery or radiation, BPH and prostate surgery, and recurrent UTI.
- Use of diuretics, poorly controlled diabetes, excessive fluid intake, mild diuretics like caffeine (e.g., coffee, cola) can precipitate urinary incontinence.
- A continuous leakage of urine with continuous wetting in a reproductive age woman should be considered to be due to fistula (**vesicovaginal**

fistula).

CLINICAL FEATURES

Symptoms

- **Encourage patients or family members to have a voiding diary:** see the table below for a typical voiding diary. If 3-7 days are recorded, it will b

Table 9.7. Template for voiding diary

1. Daytime frequency (number of urinations in 24hour):
   ____
2. Nocturia (Number of times awakened at night for urination):
   ____
3. Total volume voided in 24 hours: _________________________
4. Leakage with urgency in 24hour period: ___________________
5. Leakage without urgency in 24hour period: ______________________
6. Continence aids(pads/diapers): ___________________________________
7. Total fluid intake (water, coffee, tea, local alcoholic drinks, beer, others):
   ____

Table 9.8. Classification, mechanism and symptoms of urinary incontinence

Type of urinary incontinence	Description	Mechanism	Symptoms
Stress incontinence	Intermittent UI that occurs when there is increased intraabdominal pressure e.g., sneezing, coughing, laughing, jumping	Urethral sphincter or pelvic floor weakness	○ Leakage of small urine during physical activity or increased intra-abdominal pressure (coughing, sneezing, jumping, lifting, exercise). ○ It can occur with minimal activity such as rising from a chair
Urge incontinence	Intermittent UI experienced following a feeling of urgency. It is also called overactive bladder with incontinence.	An overactive bladder caused by irritation or loss of neurologic inhibition	○ Leakage of urine preceded by a sudden and intense desire to urinate. ○ The loss of urine occurs on the way to the toilet ○ The urgency may also be stimulated by a change in body position or sensory stimulation (e.eg. running water, cold weather, arriving at front door of the house),
Mixed incontinence	A mixture of urge and stress incontinence.		○ Leakage of urine that occurs with sensation of urgency as well as with coughing, sneezing, lifting, jumping. ○ Patients should be encouraged to identify the predominate symptom.

Overflow incontinence	A continuous leakage (dribbling) of urine due to over distended (full) bladder.	Occurs in patients with bladder outlet obstruction e.g. BPH or decreased detrusor contractility (flaccid bladder)	○ Dribbling of urine, inability to empty bladder, weak or intermittent urinary stream, hesitancy, frequency, and nocturia. ○ The postvoid bladder volume is generally >200ml. ○ Underlying diseases such as BPH, pelvic organ prolapse, neurologic disease should be sought,
Functional incontinence	It is a UI that occurs due inability or unwillingness to go to toilet because of physical disability, cognitive impairment, psychological or environmental factors.		○ Cognitive impairment such as dementia, physical impairment, immobility, mental health issues such as major depression will be seen.

Signs

- The following are important physical examinations needed in the evaluation of patients with urinary incontinence.
    - ○ **Abdomen:** Distended (palpable bladder) indicates overflow incontinence.
    - ○ **Rectal examination**: reduced or absent anal sphincter tone indicates peripheral neuropathy (causes flaccid bladder and overflow incontinence). Enlarged prostate indicates BPH (overflow incontinence)
    - ○ **Pelvic examination**: prolapse (uterine, bladder) indicate pelvic floor weakness, pelvic mass (urge or overflow incontinence)

- **Neurologic examination:** impaired mental status or cognition or paralysis can result in functional incontinence or urge incontinence, decreased perianal sensation and depressed deep tendon reflexes.
- **Musculoskeletal examination:** evidence of decreased mobility, arthritis or deformity (functional incontinence)
- **Pulmonary examination:** evidence of chronic obstructive pulmonary disease/chronic cough (stress incontinence)
- **Additional important examinations(tests)**

I. Cough stress test:

- **How to perform?**
  - Bladder: full bladder
  - Position: The patient in standing position with legs apart with a paper sheet or dry cloth on floor or in in Lithotomy position.
  - Cough forcibly: the patient relaxes pelvic muscles and cough intensely once
- **How to interpret?**
  - Leakage of urine immediately with the cough (Positive test) indicates stress incontinence.
  - Delayed leakage (after 10 seconds) or no leakage is negative. It can be false negative due to empty bladder, less intense cough or may indicate urge incontinence.

II. Measuring postvoid residual (PVR) urine volume

- **To whom**
  - PVR urine volume needs to be measured in patients who have voiding symptoms (sensation of incomplete voiding, hesitancy, poor urine stream, frequency)
- **How to perform?**
  - Ask the patient to void as completely as possible in toilet.

  - Perform sterile catheterization immediately after returning from toilet.
  - Measure the urine volume collected.
  - Alternatively, bladder volume can be estimated using ultrasound (prevoid and postvoid volume will be measured using

- ○ **How to interpret?**
  - A postvoid urine volume>100ml is considered abnormal. However, overflow incontinence happens if the volume is >200ml. If PVR volume is 100-200ml, repeat the test at another time.

Diagnosis and investigation

Diagnosis

- The diagnosis of urinary incontinence requires looking for (encouraging) patients to tell, assess its impact on quality of life, classify the type, and identify possible causes and predisposing factors. Hence, history is the most important tool in the diagnosis followed by focused physical examination.
- Structured questions like the 3 incontinence questions are helpful in improving diagnosis

The 3 Incontinence Questions

#1. During the past three months, have you leaked urine (even a small amount)?

Yes

No …. If the answer is no, do not proceed to the next questions

#2. During the past three months, did you leak urine: (check all that apply)

A. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercising?

B. When you had the urge or the feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?

C. Without physical activity and without a sense of urgency?

#3. During the past three months, did you leak urine most often: (check only one)

A. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercising? …. Stress incontinence

B. When you had the urge or feeling that you needed to empty your bladder, but you could not get to the toilet fast enough? Urge incontinence

C. About equally as often with physical activity as with a sense of urgency? …..Mixed

D. Without physical activity and without a sense of urgency? other causes

Adapted from Brown JS, Bradley CS, Subak LL, et al.; Diagnostic Aspects of Incontinence Study (DAISy) Research Group. The sensitivity and specificity of a simple test to distinguish between urge and stress urinary incontinence. Ann Intern Med. 2006;144(10):716.

INVESTIGATIONS

- **Urinalysis:** to look for evidence of infection
- **Renal function test**
- **Abdominopelvic ultrasound**: If obstructive uropathy, pelvic mass or

prostate pathologies are suspected or measurement of postvoid residual volume.

- **Urodynamic study:** not routinely needed for most patients and not readily available.

TREATMENT

Non-pharmacologic treatment

- **Use strategies to keep the patient dry (Containment)**
    - Patients should be encouraged to use pads or garments (homemade or commercial)
    - Pads or protective garments should be changed frequently to avoid irritation.
- **Life style changes**
    - Weight loss in overweight or obese patients
    - Decrease fluid intake: Don't take more than 2liters of fluid per day
    - Decrease or avoid coffee, alcohol or caffeinated beverages.
- **Physical and behavioral therapies**
    - **Kegel exercise (Pelvic floor muscle training) for stress or mixed incontinence**
        - Help the patient isolate pelvic muscles (avoid thigh or buttocks muscles). These muscles are the same muscle used to stop urine.
        - Perform 10 contractions sustained for 8-10 seconds at maximum strength.
        - Repeat the contractions at least 3 times per day. Encouragement and follow up needed
    - **Bladder training: Scheduled (Timed voiding) for urge/mixed incontinence**
        - Use the voiding diary to identify the shortest time interval.
        - Go to toilet at timed intervals decided based on the dairy (e.g. every 2 hours).

    - If timed voiding works, increase the intervals by 15minutes until 4hour is achieved or comfortable.
    - If the patient has impaired cognition, a caregiver prompts them to do it timely.
  - If urgency comes before the schedule, use behavioral distractions (relax, take deep breath, and distract yourself focusing on something else), don't rush to the toilet, sit and stand slowly and try to go to toilet relaxed.
- **Review drugs and modify:** Drugs like diuretics, sedatives, antihistamines, benzodiazepines should be decreased or avoided if possible.

PHARMACOLOGIC TREATMENT

- **Drugs for urge incontinence**
  - **First line:** Antimuscarinic drugs
    - **Oxybutynin:** starting dose 2.5mg BID to TID. Maximum dose 5mg QID

      OR

    - **Tolterodine:** starting dose: 1mg BID and increase to 2mg BID
    - The major adverse effects are dry mouth, blurred vision, delirium, constipation
  - **Alternatives** (poorly effective and higher side effects)
    - **Imipramine:** start with 12.5mg at bedtime. Gradually increase to 50mg at bedtime.
    - The major adverse effects are dry mouth, constipation, delirium, sleepiness, and postural BP drop.
- **Drugs for stress incontinence**
  - **Duloxetine:** Starting dose 20mg BID. Gradually increase to 40mg BID
  - The major adverse effects are drowsiness, headache, insomnia, anxiety, fatigue, and dry mouth

- **Drugs for mixed incontinence;** treat based on the predominate type
- **Drug for troublesome nocturia**
    - **Desmopressin (oral):** start with 0.2mg at bed time. Maximum 0.6mg at bed time.

      OR
    - **Desmopressin (intranasal):** 0.83microgram in one nostril only at bed time. Maximum 1.66microgram.
    - The major adverse effect of desmopressin is hyponatremia. Hence patients should restrict water intake and serum sodium should be monitored.
- **Treatment of urinary tract infection**
    - Provide antibiotics if there is evidence of culture proven infection or fever.
    - Don't prescribe antibiotics to patients with chronic incontinence, just because of the incontinence only.

REFERRAL:

- Indications for referral to urologist or gynecologist
    - Incontinence with new onset neurologic symptoms
    - Incontinence with vesicovaginal fistula, pelvic organ prolapses
    - Pelvic pain associated with incontinence
    - Enlarged prostate or postvoid residual volume >200ml
    - Gross hematuria associated with incontinence

FURTHER READING

1. F.C. Burkhard, J.L.H.R. Bosch, F. Cruz, G.E. Lemack et. al. European Association of Urology (EAU) Guidelines on Urinary Incontinence, Limited Text Update March 2017.

2. Raveen Syan and Benjamin M. Brucker. Guideline of guidelines: urinary incontinence. BJU Int 2016; 117: 20–33.
3. Christine Khandelwal, And Christine Kistler. Diagnosis of Urinary Incontinence. American Family Physician www.aafp.org/afp Volume 87, Number 8; April 15, 2013.

9.7 UROLITHIASIS/NEPHROLITHIASIS

BRIEF DESCRIPTION

- Urolithiasis/nephrolithiasis is a common problem in primary care practice.
- Stone formation occurs when normally soluble materials like calcium, oxalate or uric acid supersaturate (accumulate above the solubility capacity) and form small crystals.
- These crystals form a nidus for stone formation.
- Most stones (about 80%) are calcium based (calcium oxalate, calcium phosphate or a combination). Uric acid, struvite (magnesium ammonium phosphate), cystine, and others contribute to the rest.
- Stones may be symptomatic or asymptomatic.
- In some patients' stone can cause severe damage to one or both kidneys through obstruction and might result in end stage kidney disease.
- Patients who have had a history of stone have a very high risk of recurrence. By five years about half of the patients will have at least one recurrence.

Table 9.9. Risk factors for recurrent stone formation

Dietary factors	**Urinary factors**	**Family and genetic factors**	**Diseases/ comorbidities**	**Structural**
Low fluid intake	Low urine citrate	Family history	Hyperparathyroidism	Horseshoe kidneys
Low calcium intake	High urine calcium	Early onset (children and teenagers)	Diabetes Mellitus	Ureteral strictures
High salt (sodium) intake	Low urine volume	Primary hyperoxaluria	Obesity	
High oxalate intake		Cystinuria	Inflammatory bowel disease or short bowel	
			Gout	
			Recurrent pyelonephritis	

- Stones may be symptomatic or asymptomatic.
- In some patients' stone can cause severe damage to one or both kidneys through obstruction and might result in end stage kidney disease.
- Patients who have had a history of stone have a very high risk of recurrence. By five years about half of the patients will have at least one recurrence.

CLINICAL MANIFESTATIONS

Symptoms: The following are possible presentations of patients with urolithiasis

- **Asymptomatic**

  - In a significant number of patients Urolithiasis is identified incidentally when imaging is done for other indications.
- **Acute renal colic**
  - Renal colic is the most typical and severe manifestation of urolithiasis.
  - Presents with intense paroxysmal pain in area between the flank and the groin. The location changes as the stone migrates down the urinary tract
  - It can radiate to the ipsilateral testicles or labium.
  - Associated nausea, vomiting and sweating are common.
- **Non-colicky flank/groin pain**
  - Some patients may have non-colicky intermittent flank pain the may radiate to the ipsilateral groin area
- **Hematuria**
  - Gross or microscopic hematuria can be presentation
- **Passage of gravel (stone)**
  - Some patients may present with the passage of gravel.
- **Other manifestations**
  - Lower ureteric and bladder stones may present with dysuria, slow and painful micturition (stranguria)

SIGNS

- Costovertebral angle tenderness
- Observation of passed gravel (stone)

DIAGNOSIS AND INVESTIGATION

Diagnosis

1. Imaging

- The diagnosis of urolithiasis needs imaging.

- Imaging is not only needed to confirm the diagnosis but also to know the size of the stone (crucial to decide on management), the location, and the presence/absence of hydronephrosis/hydroureter.
- **Which imaging modality?**
  - **Non-contrast enhanced CT-scan** of the kidney-ureter-bladder (KUB)
    - Non-contrast enhanced CT scan is the best imaging modality
    - It has the highest sensitivity and specificity. It also detects complications and has much better sensitivity to ureteric stones.
    - It can be done with low dose radiation.
    - Request as: non-contrast-enhanced KUB CT-scan, with low dose radiation
  - **Ultrasound**
    - Ultrasound is preferred when CT-scan is not available, not-affordable, in pregnant women and children.
    - A bedside ultrasound can be used as initial evaluation to be followed by CT-scan.
    - Ultrasound has a very low sensitivity to ureteric stones, marked inter-observer variation and low accuracy for estimating size of stone (which is crucial for management decision)
  - **Plain KUB x-ray**
    - Plain KUB x-ray should not routinely be done unless there is no CT-scan or ultrasound.
    - It misses radiolucent stones and smaller stones.
  - **Intravenous urography or pyelography (IVU/IVP)**
    - It should not be routinely done at primary care level.
    - It is associated with high radiation exposure, higher cost and contrast associated complications.

  - It is largely replaced by CT-scan.

OTHER INVESTIGATIONS

- **Urinalysis:** Look for nitrite, urine PH, pyuria and hematuria
- **Urine culture:** If infection is suspected urine culture should be sent before initiation of antibiotics.
- **Renal function test: Serum creatinine and urea**
- **Serum calcium**
- **Serum uric acid level**
- **24-hour urine collection:** calcium, oxalate, citrate, uric acid, and potassium are needed in the evaluation of recurrent stone formers.
- **Parathyroid hormone level:** If hypercalcemia is found or there are other evidences of hyperparathyroidism.
- **Stone composition analysis:** it may be needed in recurrent stone formers to advise on prevention.

TREATMENT

PHARMACOLOGIC TREATMENT

1. Treatment of acute renal colic

- ○ Hospitalize those who cannot tolerate oral intake until pain subsides.
- ○ First line: parenteral NSAIDS (non-steroidal anti-inflammatory drugs).
  - – NSAIDS are better than opioids for both pain relief and decreasing the need for additional analgesics.

    Diclofenac 75mg, IV or IM stat.
  - – If parenteral formulation is not available, rectal suppositories can be used (**Diclofenac 100mg, rectal suppository or indomethacin 100mg, rectal suppository stat)**
  - – Give additional oral or rectal suppository for 3-5 days to be

taken at home if pain recurs.

  - NSAIDS should be avoided if there is known impairment in kidney function.

- **Second line: Opioid analgesics**
  - Opioids or opioid like analgesics (like Tramadol) are indicated if NSAIDS are contraindicated or if pain persists or recurs after using NSAIDS.

Morphine 2.5mg to 5mg IV, **stat** to be repeated after 3-4hours

Or

Tramadol 50-100mg IV, slowly or IM stat.

Avoid using Pethidine both as first line or second line. It is associated with much higher incidence of nausea, vomiting and increased need of a second analgesic.

- **Pain management strategies which are not useful**
  - Antispasmodics like hyoscine are not helpful in the pain management
  - Increasing **oral fluid intake or IV fluids** to facilitate stone passage is not recommended during acute renal colic episode.
- **Follow up imaging**
  - Follow up imaging (ultrasound) needs to be done in 1-2 weeks interval to assess the passage of stone and hydronephrosis

2. Facilitating stone passage (Medical expulsive therapy)

- Size of the stone and the presence or absences of hydronephrosis are the two important determinants of subsequent management of stone.
- For patients on medical therapy, regular follow up imaging need to be done.

- **Hydronephrosis: refer to urologist**
- **Size**
  - <5mm: Medical therapy with follow up
  - 5-10mm: Medical expulsive therapy with follow up
  - >10mm: Refer to urologist

- **First line drugs for medical expulsion therapy:** All patients who are managed medically should be offered the following medications.
  - **Alpha-1-blockers:**
    - ✓ **Tamsulosin 0.4mg po/day.** Stop after expulsion of the stone

      OR

    - ✓ **Alfuzosin 10mg po/day**. Stop after expulsion of the stone.
- **Second line drugs for medical expulsion therapy:**
  - **Nifedipine retard tablet 20mg once/day.**

3. **Prevention for recurrent stone formers:** pharmacologic prevention should be offered if stone formation is confirmed to be recurrent
   - Recurrent calcium-based stone:
     - **Hydrochlorothiazide 25mg/day.** The dose can be increased to 50mg/day for this indication, if serum potassium and BP are closely monitored.
   - Elevated serum uric acid, irrespective of the stone type:
     - **Allopurinol 100mg/day**

Non-pharmacologic interventions for prevention of recurrence: For all patients irrespective of stone type

Table 9.10. Non-pharmacologic interventions to prevent stone recurrences

General measures	**Specific preventive measures**	**Comments**
Increase fluid intake	• Fluid amount: 2.5-3.0 L/day • Urine amount: 2.0 -2.5 L/day	Spread throughout the day
	• Type of fluid: Any fluid but avoid sweetened carbonated beverages.	
	• Urine specific gravity to be achieved <1.010	
Nutritional advice	• Food rich in vegetables and fiber	
	• Do not decrease calcium: Normal calcium content	• Most practitioners mistakenly restrict calcium. • Calcium restriction paradoxically increases stone formation
	• Decrease salt intake	
General life style advice	• Encourage weight loss if obese or overweight • Encourage exercise	• Advice to take adequate fluid during exercise

REFERRAL

- Patients with either of the following should be referred to a urologist without delay
    1. Presence of hydronephrosis
    2. Stone size >10mm(1cm)
    3. Stone size 5-10mm and failure of medical therapy
    4. Stone in a single (single) functional kidney
    5. Non-resolving pain despite optimal pain management
    6. Signs of infection in patient with stone>5mm or hydronephrosis (it could be pyonephrosis)

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CHAPTER 10:

RHEUMATOLOGIC DISORDERS

10.1 OVERVIEW ON CONNECTIVE TISSUE DISEASES

BRIEF DESCRIPTION

- Autoimmunity refers to immune response directed against self-antigens.
- Autoimmune diseases are wide range of pathologic conditions, over eighty, caused by immune response directed against self-antigens.
- Connective tissue diseases and vasculitis are systemic rheumatic disorders with wide spectrum of clinical presentations.

Major connective tissue diseases and vasculitis

I. **Connective tissue diseases (collagen vascular diseases)**
  A. Systemic lupus erythematous (SLE)
  B. Rheumatoid arthritis
  C. SjÖgren's disease
  D. Systemic sclerosis (scleroderma)
  E. Idiopathic inflammatory myositis (Pyomyositis/Dermatomyositis/Inclusion body myositis)
  F. Mixed connective tissue disease
  G. Undifferentiated connective tissue disease

II. **Vasculitis**
  A. Large vessel vasculitis:
  ○ Takayasus's arteritis
  ○ Giant cell arteritis
  B. Medium vessel vasculitis: Polyarthritis nodosa
  C. Small vessel vasculitis:
    ○ ANCA (anti-neutrophil cytoplasmic antibody) associated vasculitis
    ○ Henoch SchÖnlein Pupura
    ○ Cryoglobulinemic vasculitis
    ○ Urticarial vasculitis

CLINICAL FEATURES

When to suspect connective tissue disease?

- Systemically unwell with constitutional symptoms: fatigue, fever, weight loss
- Cutaneous manifestations: Photosensitivity, skin rashes, alopecia, tightening skin
- Arthralgia or arthritis: Joint pain, swelling, morning stiffness
- Raynaud phenomenon: episodic blanching of the digits with cold exposure
- Serositis: pleurisy, pericarditis with or without effusion, ascites
- Muscle weakness: Proximal muscle weakness
- Sicca symptoms: Dry mouth, dry eyes
- CNS: stroke in young, vascular dementia in young, Cognitive impairment and behavioral change
- Hematologic: unexplained cytopenias, thrombosis
- Obstetric: recurrent pregnancy loss
- Sex predilection: most of the connective tissue diseases are common in women

INVESTIGATIONS AND DIAGNOSIS

- CBC: for leukopenia, anemia, and thrombocytopenia. Eosinophilia is also a common finding.
- Inflammatory markers: CRP or ESR
- Urinalysis: proteinuria, hematuria
- Serum Creatinine
- Autoantibodies: ANA, anti-dsDNA, Rheumatoid factors
- Chest X-ray: pleural effusion, infiltrates
- How is diagnosis made?

- High index of suspicion: many of the manifestations may be non-specific, hence high index of suspicion is needed
- Diagnosis is mainly syndromic: based on constellation of clinical features and supportive laboratory findings
- Diagnostic/classification criteria:
  - They are designed for creation of homogenous patient population for study purposes.
  - Most of them can be used for clinical diagnosis with a reasonable sensitivity and variable specificity.
- Autoantibodies
  - Autoantibodies are useful but not diagnostic.
  - Autoantibody tests should be sent in the appropriate clinical scenario, as some antibody tests (RF, ANA) are non-specific and can be positive in healthy individuals in the general population.
- Presentation can be insidious: few features manifesting early but gradually additional symptoms appear.
- Presentation could be acute and life threatening or organ threatening e.g. glomerulonephritis, cerebritis, respiratory failure. Treatment should be started urgently.

TREATMENT OPTIONS

- List of drugs commonly used in the management
  - Non-steroidal ant-inflammatory drugs: for mild musculoskeletal symptoms
  - Glucocorticosteroids: First line therapy for initial treatment due to their rapid anti-inflammatory effects
  - Chloroquine: useful in the management of many of the connective tissue disease. Annual ophthalmologic follow up is needed
  - Immunosuppressive

  - Methotrexate,Azathioprine, Mycophenolate Mofetil, cyclophosphamide
  - They are used in severe disease for either induction of remission, maintenance therapy or as steroid sparing.

REFERRAL

- Many patients with connective tissue diseases suffer from delayed diagnosis, wrong diagnosis and delayed referrals.
- When diagnosis is suspected, patients should be referred early.

10.2 GOUT

BRIEF DESCRIPTION

- Uric acid is a byproduct of purine metabolism. Most of the purine is produced endogenously by the liver and a lesser part comes from consumption of purine rich food.
- Gout is a common inflammatory arthritis resulting from deposition of crystals of urate in the joint space and tissues around the joint.
- Urate crystals are formed as a consequence of long-term elevation of serum uric acid levels in a predisposed individual.
- Recurrent gout attack can cause joint damage, additionally it can result in:
  - Tophus (pleural form, Tophi): accumulation of urate crystals in subcutaneous tissue, cartilage and soft tissue areas.
  - Kidney stones: formation of urate stones in the kidneys and urinary tract
  - Urate Nephropathy
- Although the prevalence of gout is not studied in Ethiopia, it is one of the commonest causes of inflammatory arthritis observed in clinical practice.
- Obesity, hypertension, diabetes, the metabolic syndrome and chronic kidney disease, alcoholism are common risk factors for Gout. Hence, all patients with diagnosis of Gout need to be screened for these risk factors.

- Males are much more commonly affected than females. It is rare to find gout in reproductive age woman, after menopause the difference between men and women narrows.
- Even though hyperuricemia is the cause gout, only 10-15% of patients with hyperuricemia develop gout.
- Most patients with hyperuricemia don't develop clinical Gout in their life time. Due to this fact hyperuricemia should not be considered equivalent to Gout.

CLINICAL FEATURES

- The clinical manifestations of Gout are classified in three
  - Acute attacks (flares)
  - Intercritical gout (periods between flares)
  - Chronic Gout (Chronic Gouty arthropathy) with or without tophi

A. Acute attacks (flares)

Symptoms

- Severe (excruciating) pain over a joint associated with swelling, redness, and hotness.
- The pain is acute in onset and reaches to its maximum within 6-12hours, not exceeding 24hours.
- Initial attacks involve a single joint. Rarely multiple joints may be involved.
- The majority of the first attacks involve the base of the great toe (known as podagra) or knee.
- Flares usually subside within several days without treatment and few days with treatment.
- Patients might perceive the initial attack as an unnoticed trauma.
- The course of gout after the first attack is variable. Some might have no recurrence while other might have frequent or occasional recurrences.

- Multiple joint involvement and upper extremity involvement at initial presentation should prompt investigation for other causes of polyarthritis.
- Most patients do not have any symptoms in the period between flares.

SIGNS

- A swollen, tender, erythematous joint and evidence of joint effusion.

B. Inter-critical gout (periods between flares)

- Even after a severe flare most patients enter in to a completely asymptomatic period.
- The presence of a completely asymptomatic period is unusual in other causes of arthritis, hence helps for diagnosis.

C. Chronic Gouty arthropathy/ Tophaceous gout

SYMPTOMS

- Chronic joint pain of variable severity involving few or many joints
- Acute flares of variable frequency on top of chronic joint pain
- Deformity of joints with limitation of movement

SIGNS

- Joint deformity and swelling
- Tophi
    - Painless (non-tender), visible and palpable swelling usually present around the joints, tendons or the ears.
    - When tophi stretch the skin their white to yellow color might be visible

INVESTIGATION AND DIAGNOSIS

Diagnosis of gout flare

- The gold standard for the diagnosis of gout in the demonstration of urate crystals from aspirated joint fluid using polarized light microscope. However, that is not possible in primary care.

- Joint fluid aspiration and analysis is mandatory if septic arthritis is considered.
- The diagnosis of acute gout flare is commonly made using history, physical examination and limited laboratory test.

Helpful clinical clues for diagnosis of acute gout flare

- ○ Male sex
- ○ Previous history of monoarticular acute onset joint pain
- ○ Time to maximum pain < or = 24hr
- ○ No symptoms in between attacks
- ○ Joint swelling with redness
- ○ Cannot bear touch or pressure on affected joint
- ○ First toe involved currently or history of involvement
- ○ Presence other risk factors (e.g., hypertension, obesity, diabetes)
- ○ Elevated current or previous serum uric acid (greater than 6mg/dl)

- Role of serum uric acid level
  - ○ During acute attacks serum uric acid can be high, normal or low.
  - ○ Normal or low uric acid is common during acute attacks.
- Role of imaging during acute flares: in acute attacks imaging has limited role

DIAGNOSIS OF INTER-CRITICAL AND CHRONIC GOUT

- The diagnosis of Inter-critical and chronic gout depends on clinical, serum uric acid and imaging findings
  - ○ The presence of recurrent flares and asymptomatic period
  - ○ Presence of tophi
  - ○ Elevated serum uric acid level
  - ○ Imaging

  - X-ray: punched out lesion, intra-osseous lesions and sclerotic overhanging edges, joint space is preserved and narrowing occurs late. Calcified tophi on soft tissue and joint area
  - Ultrasound of joint/s: useful in the diagnosis, if done with experienced hands.
- **Evaluation of associate risk factors**
  - All patients with gout need to be screened for cardiovascular risk factors: fasting blood sugar and/or HbA1c, lipid profile, and serum Creatinine.

TREATMENT

OBJECTIVES OF TREATMENT

- Relieve pain immediately during acute attacks
- Prevent recurrent attacks
- Reduce long-term joint damage
- Reduce or eliminate tophi formation
- Cardiovascular risk reduction

PHARMACOLOGIC TREATMENT

TREATMENT OF ACUTE ATTACKS (FLARES)

FIRST LINE TREATMENT FOR ACUTE ATTACKS

- In individuals with normal kidney function: NSAIDS
  - Full anti-inflammatory dose needed
  - There is no evidence to show one NSAID is clearly superior to another.
  - NSAIDS should be avoided in patients with impaired kidney function, active peptic ulcer disease and cardiovascular disease.

Table 10.1 Treatment of acute attacks (flares)

NSAIDs	Dosage	Duration	Precautions
Indomethacin	Oral: 50mg, TID -Maximum dose 200mg/day	- Total duration x 7 days -The initial high dose can be reduced after 2-3 days	-PPI prophylaxis should be given for prevention of GI bleeding in the following group ○ Age ≥60 ○ Dyspepsia history in any age group ○ Concurrent use of Aspirin, anticoagulant or steroid
	Rectal suppository: 100mg/day		
Diclofenac	Oral: Immediate release 50mg, TID Extended release 75mg, BID Maximum dose: 150mg/day		
	Rectal suppository: 100mg/day		
	Intramuscular: 75mg, IM, BID		
Ibuprofen	Oral: 800mg PO TID - Maximum dose 3,200mg/day		
Meloxicam	Oral: 15mg/day - Maximum dose 15mg/day		

- In individual with impaired kidney function: short course steroids are first line
    - ○ **Prednisolone**, 30mg per day, to be tapered over 10-14 days.
        - – Typical prescription: 30mg x3days, 20mg x3days, 10mg x3days, 5mg x3days

- Intramuscular steroid/Intra-articular steroid: If oral prednisolone is not tolerated
- **Triamcinolone acetonide 40-60mg,** IM, stat. For intra-articular 40mg for large joints and 20mg for small joints.
- **Methylprednisolone 40-80mg,** IM, stat. For intra-articular 40mg for large joints and 20mg for small joints, intra-articular, once

- In patients with diabetes, worsening of hyperglycemia should be anticipated and doses of diabetes medication needs to be adjusted accordingly.

SECOND LINE TREATMENT FOR ACUTE ATTACKS

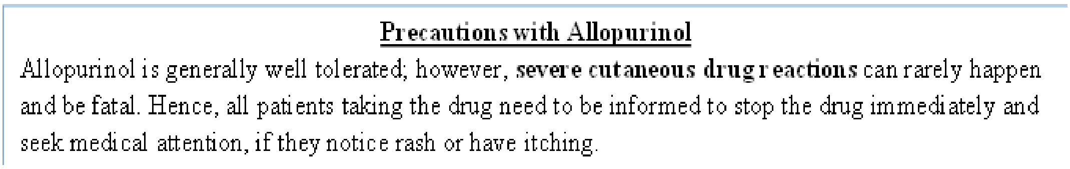
- If there is no impairment in kidney function: Colchicine
  - **Colchicine**: Initial dose of 1.2mg, after one hour 0.6 mg, a total dose in the first day
    - Subsequent dose: 0.5 to 0.6mg daily to twice daily
    - Duration: Until symptoms subside
    - GI intolerance, mainly diarrhea and to a lesser extent vomiting are common adverse effects of colchicine

URATE LOWERING THERAPY:

- for prevention of recurrence, joint damage and renal complication
- Indications for starting urate lowering therapy: Any one of the following are indication to start urate lowering therapy
  - Recurrent acute flares (> 2 flares in one year)
  - Presence of tophi
  - Chronic joint damage: Clinical or radiologic
  - Renal stones in patients with hyperuricemia
  - First attack in patients who need continuation of diuretics
- First line urate lowering therapy

  - Allopurinol is the first line urate lowering therapy
  - Start after two weeks of flare
  - Dose escalation: Dose should be escalated every 2-4 weeks, until target uric acid level is achieved.
  - Starting dose in patients with normal kidney function: **Allopurinol 100mg/day**
  - Dose escalation: Increase by 100mg every month until target serum uric acid level is achieved to a maximum dose of 800mg/day.
  - Most patients require about 300mg/day or above.
  - Once target serum uric acid level is achieved: follow up can be done every 4-6 months
- Dose of Allopurinol in patients with significantly impaired kidney function

  - Starting dose
    - eGFR 5–15ml/min: 50 mg twice weekly
    - eGFR 16–39ml/min: 50 mg every 2 days
    - eGFR 31–45ml/min: 50 mg daily
  - Maximum dose for patients with eGFR<30m/min 300mg/day



Precautions with Allopurinol

Allopurinol is generally well tolerated; however, **severe cutaneous drug reactions** can rarely happen and be fatal. Hence, all patients taking the drug need to be informed to stop the drug immediately and seek medical attention, if they notice rash or have itching.

- Target serum uric acid level
  - Non-Tophaceous Gout: less than 6mg/dl
  - Tophaceous gout: less than 5mg/dl
- Prophylaxis for flares during urate lowering therapy
  - During initiation and dose escalation of Allopurinol gout flares are

common
    - o Prevention of flares is needed during the first 06 months of Allopurinol therapy.
    - o First line for patients with normal kidney function: Colchicine 0.5 to 1mg/day
    - o First line for patients with impaired kidney function: Prednisolone 5 to10mg/day
    - o Alternative for patients with normal kidney function, if cardiovascular risk is lo: low dose NSAIDs with PPI (e.g., **Diclofenac 50mg -75mg/day, Ibuprofen 200-400mg BID)**
    - o In situations when colchicine or NSAIDs are not tolerated/not available/contraindicated: Prednisolone 5 to10mg/day

NON PHARMACOLOGIC MANAGEMENT OF GOUT

- Non- pharmacologic management is essential in all patients with gout. The non-pharmacologic management includes the following three elements:
    - o Dietary management
    - o Life style management and screening for cardiovascular risk factors
    - o Education
- Dietary management
    - o Dietary management alone is insufficient to control gout but it is an important adjunct.
    - o Excessive focus on dietary management without using effective urate-lowering therapy should be avoided.

Table 10.2: Foods which need to be restricted

Foods which need to be restricted	Remark
Meat	There is no difference among the red meat types (beef, lamb, goat meat or mutton)

Alcoholic drinks including beer	Red wine in moderation has the lowest risk
High sugar containing drinks and foods	

Table10.3: Foods that should encourage or not restricted

Foods should encourage or not restricted	Remark
Milk and dairy products	Encourage
Fruits and vegetables	Encourage
Egg	Encourage
Bean, peas, chickpea	Safe and can be taken safely

- Life style management and cardiovascular risk screening
    - Weight reduction should be encouraged in overweight and obese individuals.
    - All patients with gout should be screened for hypertension, diabetes, and dyslipidemia.
- Education
    - All patients with gout should be educated on flare management, the purpose and the lifelong nature of urate lowering therapy, adherence, dietary and life style management
    - Health care providers should be proactively educating patients and their families on the common misconceptions on the dietary management of gout.

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10.3. OSTEOARTHRITIS

BRIEF DESCRIPTION:

- Osteoarthritis (OA) is a joint disease which results from an active pathology involving the whole joint structure including cartilage damage, low grade joint inflammation, bone remodeling, and osteophyte formation.
- It was previously thought that OA is a degenerative disease; however, it is now understood that it is the result of active biochemical and cellular pathologic process.
- Joint pain and progressive loss of joint function result from the pathologic process.
- The knee, hip and hand joints are the most commonly affected sites.
- OA is considered to be the leading cause of join related disability in old adults.
- Common risk factors for OA are: old age, overweight/obesity, female sex, occupation, and injury/trauma.

CLINICAL FEATURES

Symptoms

- Joint pain
    - Pain in OA is generally activity related and relived by rest. It is more intense at the start of activity.

  - It is worse in the afternoon and evening.
- Joint stiffness
  - The morning stiffness in OA is shorter (<30 minutes) compared to rheumatoid arthritis and other inflammatory arthritis.
- Symptoms of "crepitus"
  - Clicking, grinding or popping feelings
- Instability of joint**:**
  - Buckling or giving away feeling, lacking the confidence to use weight bearing joints
- Limitation of movement
- Deformity

SIGNS

- **Distribution of joint involvement:**
  - Single joint OA: knees, hips, thumb, interphalangeal joints, cervical or lumbar spine
  - Generalized (Polyarticular) OA
  - More than two joint regions are involved.
  - Symptoms usually starts in the hands around middle age and subsequently affect the knees and other joints over several years
  - The main clinical sign is the presence of multiple Heberden's nodes (hard/bony swelling in the DIP joints) or Bouchard's nodules (hard/bony swellings in PIP joints)

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of osteoarthritis is clinical.
- The presence of following three makes the diagnosis of OA highly likely:
  - I. Age ≥45 years
  - II. Joint pain in only one or few joints
  - III. Morning stiffness duration ≤30 minutes

- The presence of other clinical features e.g., Heberden's node, joint instability and crepitus makes the diagnosis of OA more certain.
- Imaging: x-ray of the involved joint is used to support the diagnosis
- ESR or CRP: Generally normal in patients with OA.
- Investigations to exclude other differential diagnoses
  - o Psoriatic Arthritis has to be ruled out in polyarticular OA,
  - o Rheumatoid factor/anti-CCP antibody if rheumatoid arthritis is suspected
  - o Joint fluid aspiration may be needed

TREATMENT

OBJECTIVES OF TREATMENT

- Pain control
- Improving quality of life and functionality

PHARMACOLOGIC TREATMENT

PAIN MANAGEMENT: FIRST LINE

- Non-steroidal anti-inflammatory drugs (NSAIDS) are first line:
- Topical NSAIDS: For knee and other joints as well OA
- Systemic NSAIDS (oral or rectal suppository) : For all types of OA including
  - o There is no significant difference in efficacy among the different NSAIDS
  - o The minimum effective dose needs to be given
  - o For patients with high risk for GI bleeding use with proton pump inhibitors
  - o NSAIDS are contraindicated in patients with history of upper GI bleeding and chronic c kidney disease

PAIN MANAGEMENT: SECOND LINE

- If NSAIDS are contraindicated or ineffective the following are considered as second line therapies
  - **Duloxetine:** Initial dose 30mg/day, increase t0 60mg/day after at least one week. Maximum dose 120mg/day
  - **Acetaminophen (Paracetamol):** 1000mg every 6-8 hours, maximum daily dose 4000mg.
  - **Tramadol:** use the lowest effective dose

Dose for immediate release: 50mg/day and increase to 50mg every 12 hours. Gradually increase to 50mg every 6 hourly. Maximum dose 300mg/day

Drugs which **are not recommended** for the management of OA

- Non-tramadol opioids
- Systemic steroids
- Colchicine
- Bisphosphonates
- Methotrexate

PAIN MANAGEMENT: INTRA-ARTICULAR STEROIDS

- Can be used for knee or hip (for hip it should only be image guided) can be given by specialist who have experience.

NON-PHARMACOLOGIC MANAGEMENT

- Exercise based non-pharmacologic treatment: The following exercise-based interventions are recommended for the treatment of OA
  - Both aerobic (e.g., walking) and local muscle strengthening are useful
  - Tai Chi (a form of Chinese martial art practice along with meditation) and Yoga
- Weight loss: For overweight individuals with knee or hip OA
- Patient education: including self-management

- Cane (walking stick), braces and orthosis
- Cane (walking sticks): for knee or hip OA
- Braces: tibiofemoral knee braces for knee OA
- Hand orthosis: For first carpometacarpal joint
- Surgical treatment
    - Total joint replacement hip or knee) can be considered in patients with end-stage OA (i.e., severe persistent symptoms and marked functional impairment).
    - Patients should be referred to specialized hospitals or centers.

The following surgical interventions are not recommended

- Arthroscopic debridement
- Abrasion arthroplasty (involving burring and drilling of sclerotic bone)
- Synovectomy

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10.4 SYSTEMIC LUPUS ERYTHEMATOUS (SLE) (LUPUS)

BRIEF DESCRIPTION

- SLE is a multi-system autoimmune disease with chronic, relapsing-remitting course and variable manifestations.
- Manifestations could range from a mild one to a life-threatening.
- The diagnosis of the disease could be challenging as it might have unpredictable course and mimic many other systemic diseases.
- SLE can affect any organ including the musculoskeletal, skin, hematologic, renal, neuropsychiatric, cardiovascular, and respiratory system.
- Not all manifestations appear simultaneously. Interval between the different manifestations could be months or years.
- Constitutional (especially fatigue), Mucocutaneous and musculoskeletal symptoms tend to occur early.
- Females are much more commonly affected than males.
- The age of onset also ranges childhood to old age. The common age of onset is third to 3rd to 5th decade.
- Renal disease is the commonest organ/life threatening involvement.
- Lupus is associated with increased risk of thrombosis and accelerated atherosclerosis
- Pregnancy increases the risk of flare and should be avoided unless the lupus in remission for more than six months.

CLINICAL FEATURES

Symptoms

- Constitutional symptoms: Fatigue, fever, weight loss
- Mucocutaneous: Increased hair loss, photosensitivity, acute or subcutaneous/subacute and chronic skin lesions

- Musculoskeletal: Joint pain/swelling, morning stiffness, deformities can also happen
- Pulmonary: Cough, shortness of breath, pleuritic chest pain
- Cardiovascular: chest pain
- Renal: body swelling, decrement in urine amount, reddish urine, foaming of urine
- Neurologic: headache, seizures, decreased cognition, changes in mental status, weakness of extremities, features of painful peripheral neuropathy
- Psychiatric: behavioral changes

SIGNS

- Mucocutaneous: malar rash, maculopapular or bullous lesions, scaring discoid rash, painless oral ulcers, non-scaring alopecia
- Musculoskeletal: joint swelling, tenderness and decreased mobility
- Pulmonary: signs of pleural effusion, pleural friction rub, crackles
- Cardiovascular: signs of pericardial effusion, pericardial friction rub
- Renal: edematous state
- Neurologic: focal neurologic deficit, low score on mine mental test
- Psychiatric: behavioral changes

INVESTIGATION AND DIAGNOSIS

Investigations

- Autoantibodies
    - ANA
    - Anti-dsDNA
    - Anti-Smith,
    - Anti-phospholipid antibodies: Lupus anticoagulant, anti-cardiolipin, beta-2 glycoprotein

- Investigations for systemic involvement
    - Hematologic: CBC (anemia, thrombocytopenia, leukopenia)
    - Renal: urinalysis (proteinuria, hematuria), 24hour urine protein (>500mg), Creatinine and urea
    - Pulmonary: Chest x-ray (pleural effusion, interstitial infiltrates)
    - Cardiac: Echocardiography
    - CNS: MRI and MRA

DIAGNOSIS

- The diagnosis of SLE is based on a constellation of clinical laboratory and autoantibody tests.
- The presence of cutaneous, musculoskeletal symptoms associated with constitutional symptoms in young or middle-aged women unless explained by another obvious diagnosis should suspected to be SLE
- A high index of suspicion is needed.
- Classification criteria
    - The two widely used classification criteria for SLE clinical diagnosis are the 2012 SLICC and 2019 EULAR/ACR
    - Both have good sensitivity and specificity; hence, it is advised to use either of them for the purpose of diagnosis in patients with clinical features suggestive of SLE.
    - 2012 SLICC: sensitivity of 96.7% and specificity 83.7%
    - 2019 EULAR/ACR: sensitivity of 96.1% and specificity of 93.4% (see the 2012 SLICC classification criteria below)

The 2012 SLICC criteria for SLE classification

Ref.: Arthritis Rheum 2012; 64:2677-2686.

1. Diagnosis requires fulfillment of at least **four criteria**, with at least one clinical criterion AND one immunologic criterion

   OR

2. Lupus nephritis as the **sole clinical criterion** in the presence of ANA or anti-dsDNA antibodies

Clinical Criteria	**Immunological Criteria**
1. Acute cutaneous lupus	1. ANA above laboratory reference range
2. Chronic cutaneous lupus	2. Anti-dsDNA above laboratory reference range, except ELISA: twice above laboratory
3. Oral ulcers: palate	3. Anti-Sm
4. Nonscarring alopecia (diffuse thinning or hair fragility with visible broken hairs)	4. Antiphospholipid antibody: any of the following
5. Synovitis involving two or more joints, characterized by swelling or effusion OR tenderness in two or more joints and thirty minutes or more of morning stiffness.	5. Low complement
6. Serositis	6. Direct Coombs test in the absence of hemolytic anemia
7. Renal	
8. Neurologic	
9. Hemolytic anemia	
10. Leukopenia (< 4000/mm3 at least once)	
11. Thrombocytopenia (<100,000/mm3) at least once	

TREATMENT

OBJECTIVES OF TREATMENT

- Improvement in quality of life
- Prevent flares
- Prevent life threatening complications

Non-pharmacologic treatment

- Exercise
- Minimization of sun exposure: hat, umbrella
- Stress management

Pharmacologic management

- **NSAIDS:** for arthralgia and mild arthritis
- **Corticosteroids:** For multiple indications
  - Pulse steroid: for acute life or organ threatening
    - **Methylprednisolone 250 -1000mg** IVX for 3 days
  - High dose steroid: for severe organ/life threatening for 4-8 weeks with tapering after that
    - **Prednisolone 0.5-1mg/kg/**day or equivalent
  - Moderate steroid: prednisolone >10 to 0.5mg/kg/day or equivalent
  - Low dose steroid (maintenance):< or =10mg
- **Antimalarial:** all patients with SLE in the absence of contraindication
  - Chloroquine phosphate 250mg/day or 250mg PO 5 times per week
  - Baseline and annual ophthalmologic screening is needed, for possible retinopathy.
- **Other immunosuppressive**:

- For life/organ threatening indication or as steroid sparing
- They should be prescribed by specialists who have experience in using them
    - Azathioprine
    - Methotrexate
    - Mycophenolate Mofetil
    - Cyclophosphamide

REFERRAL

- Patients with SLE with renal, neurologic involvement should be referred urgently. Others need to be referred on elective basis after initial management.

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10.5 RAYNAUD'S PHENOMENON

BRIEF DESCRIPTION

- Raynaud phenomenon (RP) is an exaggerated vasoconstrictive response to cold temperature and emotional stress.
- It is characterized by episodic attacks, called vasospastic attacks, that cause the blood vessels (arterioles) to constrict
- It affects 5 - 10 % of the general population
- It is usually triggered by exposure to cold or emotional stress.
- The attacks mainly affect the fingers or toes but may affect nose, lips, ear lobes, breast.
- It is classified in to two:
  - **Primary :** No associated disorder
  - **Secondary** : occurs in the presence of underlying disorder
- The major causes of secondary Raynaud are connective tissue disorders (mainly scleroderma and lupus).
- Other causes of secondary Raynaud include drugs (Cisplatin), long term use of vibration tools and carpal tunnel syndrome.

CLINICAL FEATURES

Symptoms

- During the attack the person experiences three phases of skin color changes
  - **1st White (Pallor):** vasoconstriction (ischemic phase)
  - **2nd Blue (cyanosis):** hypoxemia (ischemic phase)
  - **3rd Red (erythema)**: reperfusion
- Not everyone has all three colors.
- The order of the changes of color is not the same for all.

- Throbbing and tingling sensation.
- An attack can last from less than a minute to several hours.
- With rapid rewarming generally the attacks last 15-20 minutes

SIGNS

- Tissue ischemia (eg, ulcerations) of the hands and feet ears, nose, face, knees, and nipples.
- Signs of other connective tissue disease
    - Sclerodactyly (tightening and thickening of the skin of the fingers which can curl the finger inward) in scleroderma
    - Malar rash, alopecia, sign of joint inflammation

DIAGNOSIS AND INVESTIGATION

Diagnosis

- The diagnosis is made clinically, mainly based on history. However, all patients should have a thorough evaluation for connective tissue diseases(mainly scleroderma and lupus)
- Clinical diagnosis can be made if the patient responds yes to all three of the following
    - Are your fingers unusually sensitive to cold?
    - Do your fingers change color when they are exposed to cold temperatures?
    - Do your fingers turn white, blue, or both?

Investigations

- ANA
- CBC and ESR

TREATMENT

OBJECTIVES OF TREATMENT

- Shorten duration of attack
- Decrease recurrence of attacks
- Prevent permanent ischemic tissue damage

Non-pharmacologic management

- Educate patients on the following two aspects

I. **Preventive strategies**
  - o Keep warm
    - – Avoid cold exposure
    - – Appropriate dressing : gloves, socks, hats, and gloves or mittens
  - o Gloves before handling frozen or refrigerated foods.
  - o Quit smoking
  - o Control stress.

II. **Managing an attack**
  - o An attack should not be ignored
  - o Warm the hands or feet: run warm water or soak in a bowl of warm water
  - o Stress management: if the attack is triggered by stress Patients should be advised

PHARMACOLOGIC MANAGEMENT

- If non-pharmacologic management fails and the patient has significant recurrences
- First line: Calcium channel blockers
  - o **Nifedipine (long acting)** :

    - Starting dose 20-40mg/day single or two divide dose maximum dose 180mg/day

      OR

  - **Amlodipine**, starting dose 5mg/day, maximum dose for this indication 20mg/day

REFERRAL

- Refer patients to referral hospital if there is a consideration of secondary Raynaud's phenomenon or if symptoms of primary one are refractory.

FURTHER READING

1. Pauling, J. D., Hughes, M., & Pope, J. E. (2019). Raynaud's phenomenon—an update on diagnosis, classification and management. Clinical Rheumatology. doi:10.1007/s10067-019-04745-5

2. Fredrick M. Wigley and Nicholas A. Flavahan. Raynaud's Phenomenon. N Engl J Med 2016;375:556-65.

10.6 RHEUMATOID ARTHRITIS (RA)

BRIEF DESCRIPTION:

- Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disease mainly characterized by symmetrical polyarthritis of the small joins of hand and feet with progressive damage of joints.
- In addition to joints, it affects the lung (ILD, Pleurisy, PAH), blood (cytopenia and Felty's syndrome), skin (erythema nodosum and a variety of vasculitic lesions) and less commonly other organs.
- It more common in women than men.
- Although the onset can be at any age, the peak is 50-60 year in women and >70 year in men.

CLINICAL FEATURES

Symptoms

- Joints **symptoms**
  - The most typical symptomatic presentation of RA is that of a symmetric polyarthritis (defined as involving > 5 joints), involving small joints of the hands, wrists, and/or feet.
    - Joint pain
    - Joint swelling
    - Early Morning stiffness : usually lasts > 02 hours
    - Limitation of joint mobility (difficulty of using the joint)
- **Constitutional symptoms**
  - Some patients may have systemic symptoms in addition to the joint symptoms
    - Fatigue
    - Generalized musculoskeletal pain
    - Weight loss
- **Symptoms from other organ-system involvement (extra-articular symptoms)**
  - Occasionally patients may also present with other organ involvements:
    - Cough, shortness of breath, chest pain : Lung involvement
    - Dryness of the eyes , red and/or painful eyes: Eye involvement/
    - Swellings(nodules), red/dark lesions, ulcers on the skin: Skin/ vascular involvement
    - Numbness or pain over the extremities: Peripheral nerve involvement

Signs

- **Joint**
  - Swelling (bogy swelling from effusion or subtle swelling from thickening)

  - Tenderness
  - Deformities
- **Other organ-systems (extra-articular signs):**
  - Depending on the systems involved e.g. subcutaneous nodules, enlarged lymph nodes, signs of pleural/pericardial effusion, splenomegaly

INVESTIGATIONS AND DIAGNOSIS

- **When to suspect RA?** RA should be strongly suspected in any patient who present with multiple joint pain, swelling and morning stiffness for few weeks.
  - Hand, wrist, and foot joints are the most commonly involved; however, any joint can be involved.
  - Distal interphalangeal (DIP) joints are usually spared in RA.
  - The spine(the back), apart from the atlantoaxial joint, is not directly involved by inflammation but may be affected by osteoporosis and mechanical imbalance due to involvement of the weight bearing joints.
- **How is the diagnosis of RA made?**
  - There is no single test, imaging finding or clinical finding which is diagnostic of RA.
  - A strong clinical suspicion is needed in any patient when with polyarthritis for few weeks.
- **The role of diagnosis /classification criteria**
  - The classification criteria for RA is designed for the purposes in researches, but it is a good clinical guide to make a diagnosis with a reasonable sensitivity
- **The role of antibody tests (Rheumatoid factors (RFs) and Anticyclic-citrullinated peptide (Anti-CCP) antibodies**)?
  - Because of low sensitivity of both tests and low specificity of RFs, these autoantibodies are not alone enough for establishing diagnosis.

- With their limitations, they can help in the diagnosis and predicting prognosis.
- **Rheumatoid factors (RFs)**
  - Sensitivity: About 70% of patients are positive at diagnosis.
  - False positivity: other connective tissue diseases like SLE and some infectious diseases like malaria and hepatitis C, can cause false positive results.
  - False negativity : Nearly one third of patients with RA are negative RFs results
- **Anti-CCP antibody test**
  - Sensitivity: Similar to rheumatoid factors
  - Specificity: > 95%.
- **Other investigations**
  - ESR or CRP: Moderately increased ESR (usually not >50ml/min) or CRP. ESR and CRP may be normal in about one-third of patients.
  - CBC: Norma WBC, mild anemia (due to chronic inflammation), or thrombocytosis (due to chronic inflammation)
  - Imaging (X-ray): in early disease X-ray is usually normal, as the disease advances X-ray shows decreased bone density, bone erosion, joint space narrowing, and deformities.

ACR/EULAR 2010 Classification Criteria for Rheumatoid Arthritis

- These criteria should be restricted to persons with at least one clinically detectable swollen joint in the absence of a more likely diagnosis..
- A score of ≥6 points is classified as definite RA. In each domain, consider only the category with most points.

A. Joint involvement and distribution (0-5 points)

- Any swollen or tender joint on physical examination
- Large joints: Shoulders, elbows, hips, knees, and ankles
- Small joints: Metatarsophalangeal, proximal interphalangeal, second through fifth
- Metatarsophalangeal, thumb interphalangeal, and wrists
    - 1 large joint: 0 points
    - 2–10 large joints: 1 point
    - 1–3 small joints: 2 points
    - 4–10 small joints: 3 points
    - > 10 joints (and at least 1 small joint): 5 points

B. Serology (0-3 points)

- Low-positive results are > 1 to 3 times the upper limit of normal of the assay used.
- High-positive results are > 3 times the upper limit of normal of the assay used
    - Negative RF and negative ACCP: 0 points
    - Low-positive RF or low-positive ACCP: 2 points
    - High-positive RF or high-positive ACCP: 3 points

C. Acute-phase reactants (0-1 point)

- Normal CRP and normal ESR: 0 points
- Abnormal CRP or abnormal ESR: 1 point

D. Duration of symptoms (0-1 point)

- Patient's self-report on the maximum duration of symptoms of any joint clinically involved at the time of assessment
    - < 6 weaks: 0 points ≥6 weaks: 1 point

TREATMENT

OBJECTIVES OF TREATMENT

- Achieve remission or low disease activity disease-modifying ant rheumatic drugs (DMARDS)
- Relieving acute inflammatory pain/symptom control

PHARMACOLOGIC TREATMENT

Disease-modifying ant rheumatic drugs (DMARDS)

- All patients with RA should be started with DMARDS without any delay
- If DMARDs are not available or you don't have the experience of using them, the patient should be referred.
- First **line DMARD: Methotrexate (MTX) 7.5 to 25mg/once per week**
    - **Investigation before initiation of MTX**: CBC, liver enzymes, screening HBV and HCV, BUN and Creatinine, Chest X-ray.
    - **Starting dose:** 7.5mg -10mg per week.
    - **Route of administration:** Oral or subcutaneous
    - **Dose escalation:** The MTX dose needs to be escalated by 2.5mg-5mg, at intervals no more frequent than every month until disease activity is well controlled or maximum tolerated dose is achieved.
    - **Maximum dose:** 25mg/week
    - **Folic acid:** All patients on MTX should be given Folic acid to prevent the hematologic and other side effects.
        - Folic acid 1mg tab, PO/day or 5mg tab, PO/2-3 times per week
    - **Major adverse effects:** Liver toxicity, Bone marrow suppression (pancytopenia), lung toxicity and increased susceptibility to infection
    - **Monitoring:** All patients need to have CBC and liver enzymes (LFT) monthly for the first 3 months, then every 03 months.

- **Contraindications to MTX:** Pregnancy, significant impairment in kidney function (eGFR<30ml/min), chronic liver disease, and active/ uncontrolled infection.

ADDITIONAL OR ALTERNATIVE DMARDS

Chloroquine: Chloroquine phosphate 250mg/day

- **As additional agent:** Add Chloroquine in patients who are having poor disease control while taking maximally tolerated dose or >15mg of MTX/ week.
- **As an alternative to MTX:** In patients for whom MTX is contraindicated or have mild disease Chloroquine can be used as an alternative.
- **Dosing in adults:** Chloroquine phosphate 250mg tab (equivalent to Chloroquine base 150mg), 01 tablet 5times per week
- **Major side effects:** Ophthalmic (retinal) toxicity, neuropathy, myopathy.
- **Screening for ophthalmic toxicities:** Although it is rare, ophthalmic complication is the most feared one. Patients need to have ophthalmologic evaluation within the first year of therapy (baseline) and then annually.

DISEASE ACTIVITY NOT WELL CONTROLLED BY A COMBINATION OF MAXIMUM/ MAXIMALLY TOLERATED DOSE METHOTREXATE AND CHLOROQUINE:

- Add low dose steroid (<10mg/day) as part of the DMARD and refer to a tertiary care.

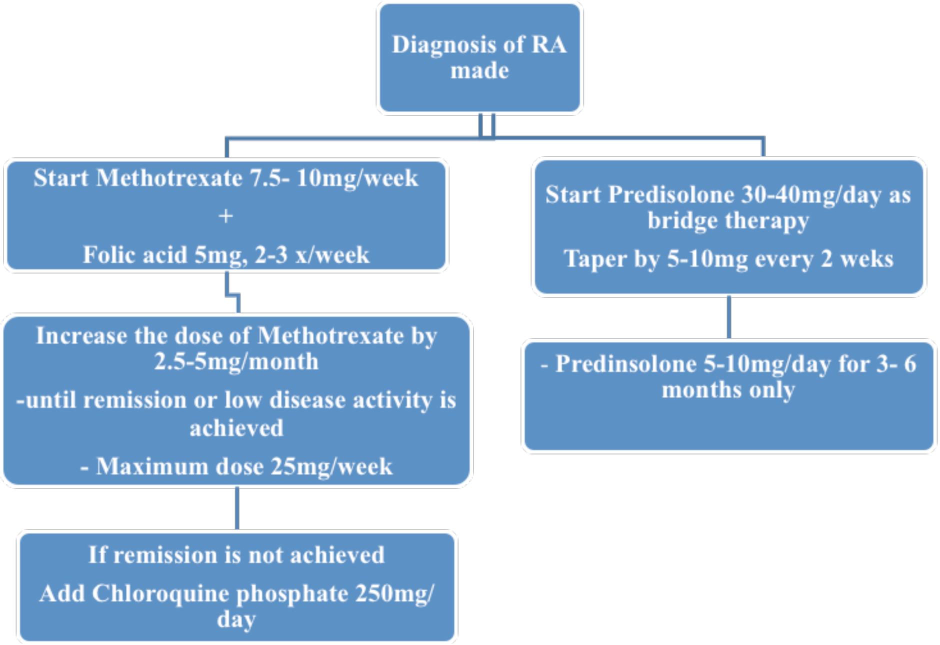
RELIEVING ACUTE INFLAMMATORY PAIN

- **First line**: Non-steroidal anti-inflammatory drugs (NSAIDS) or short course corticosteroids
  - Non-steroidal anti-inflammatory drugs (NSAIDS) options
    - **Ibuprofen,** 400-800mg, P.O, TID with meals.
    - **Diclofenac,** 150mg/day, P.O, in 2-4 divided doses. Rectal suppository 100mg/day
    - **Indomethacin,** 25-50mg P.O.TID; maximum dose: 200mg/day.

        Rectal suppository, insert 100mg, BID or once.
    - **Meloxicam,** 7.5 - 15mg/day. Maximum dose 15mg/day
    - **Piroxicam,** 10-20mg/day. Maximum dose 20mg/day
- Precautions with NSAIDS
    - Avoid **NSAIDS** in patients with impaired kidney function
    - Offer **Proton pump inhibitors (PPIs)** for those at high risk of **NSAIDs** associated peptic ulcer bleeding: patients with history of peptic ulcer symptoms, on Aspirin/anticoagulant /steroid

1.1 Corticosteroids: Indications

- **As** a bridge to DMARDS at diagnosis
    - Prednisolone
    - Starting dose: 20mg/day. Do not exceed 30mg/day.
    - Tapering: taper by 5-10mg every 2 weeks, keep it <10mg/day for 3-6 months until DMARDs take over.
- Flare management
    - Prednisolone 15 -20mg/day taper to baseline dose or stop in 2 weeks
- Chronic therapy
    - Corticosteroids are not generally regards as DMARDS
    - Long term therapy is not recommended
    - In some patients where disease activity is poorly controlled while a combination maximum/maximum tolerated dose DMARDs low dose steroid may be needed
    - Prednisolone 5-10mg/day achieved


Diagnosis of RA made
Start Methotrexate 7.5- 10mg/week
+
Folic acid 5mg, 2-3 x/week
Start Predisolone 30-40mg/day as bridge therapy
Taper by 5-10mg every 2 weks
Increase the dose of Methotrexate by 2.5-5mg/month
-until remission or low disease activity is achieved
- Maximum dose 25mg/week
- Predinsolone 5-10mg/day for 3- 6 months only
If remission is not achieved
Add Chloroquine phosphate 250mg/ day

FURTHER READING

1. Smolen JS, Landewé RBM, Bijlsma JWJ, et al.EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update.Ann Rheum Dis 2020; 79:685–99.

2. Jeffrey A. Sparks. In the Clinic Rheumatoid Arthritis. Annals of Internal Medicine Vol. 170 No. 1. 1 January 2019.

3. Josef S Smolen, Daniel Aletaha, Iain B McInnes. Rheumatoid arthritis . Lancet 2016; 388: 2023–38.

CHAPTER 11:

NEUROLOGICAL DISORDERS

11.1 DEMENTIA

BRIEF DESCRIPTION

- Dementia is a group of disorders characterized by a decline in cognition involving one or more of the cognitive domains (see table 11.2 below). There must be a decline from previous levels of cognitive function.
- The cognitive deficit must be severe enough to interfere with daily function and independence.
- The cognitive deficits should not occur exclusively in the context of a delirium and are not better explained by another mental disorder (e.g., major depressive disorder)
- Old age remains to be the most important risk factor for dementia. Young onset dementia is considered when the onset is before the age of 65.
- Other risk factors for dementia include family history, history of cardiovascular or cerebrovascular disease, diabetes, obesity, alcohol, anticholinergic medications.
- Dementia is often preceded by a period of mild cognitive impairment (MCI).However, not all patients with MCI progress to dementia.
- Mild cognitive impairment (MCI) is defined as the presence of memory impairment (both subjective and objective) but it is differentiated from dementia by the preserved function in performing daily activities.
- Delirium is an acute (hours to a few days) state of confusion with fluctuating level of consciousness in a single day.

Table 11.1. Major causes/subtypes of dementia

1. Alzheimer’s Disease
2. Vascular dementia
3. Dementia with Parkinsonism
    - Dementia Lewy Bodies
    - Parkinson’s disease dementia
    - Corticobasilar degeneration (CBD)
    - Progressive Supranuclear Palsy (PSP)
4. Fronto-temporal dementia (FTD)
5. Normal pressure hydrocephalus
6. Medical conditions
    - Alcohol-related dementia
    - HIV infection
    - Hypothyroidism
    - Depression
    - Vitamin B12 deficiency
    - Neurosyphilis
    - Medication adverse effects

CLINICAL FEATURES

- Concerns by patient’s family, caregivers or friends
- Physician recognizing declining cognitive function or aberrant patient behaviors
- Symptoms or observations related to each cognitive domain include(see the table 11.2 below).
- In addition to cognitive symptoms behavioral and psychological symptoms may be present

- Behavioral symptoms: restlessness, aggression, agitation, wandering, sexual disinhibition, restlessness.
- Psychological symptoms: anxiety, depression, hallucinations and delusions.

Table 11.2: Cognitive domain and associated symptoms of dementia

Cognitive domain	Symptoms and observations
Complex attention	○ Routine tasks take much longer time ○ Work requires more overview/rechecking than before
Executive function	○ Difficulty in completing previously familiar multistep tasks e.g. preparing a meal, wearing clothes ○ No longer wanting to participate in activities at home ○ Avoids social activities as they become less enjoyable
Language	○ Difficulty finding the correct words ○ Forgetting names: using general pronouns than names ○ Mispronunciation of words ○ Problems with understanding communication
Learning and memory	○ Difficulty in recalling recent events ○ Forgetting to buy items or buying the same items multiple times ○ Repetition in conversations

Perceptual-motor	○ Difficulty in using familiar technology, tools, or appliances ○ Getting lost in familiar environments
Social cognition	○ Apathy ○ Increase in inappropriate behaviors ○ Loss of empathy ○ Impaired judgment

INVESTIGATIONS

- All patients with dementia need the following tests
    - CBC: look for evidence of anemia and macrocytosis or pancytopenia
    - Vitamin B12 level
    - Thyroid function test: TSH
    - Renal and liver function tests
    - Screening for HIV and syphilis
- Brain imaging
    - Indicated in all patients with no clear and reversible medical causes
    - MRI is preferred over CT scan. If MRI is not available CT scan is acceptable.

DIAGNOSIS

- The diagnosis of dementia requires the following steps

1. Screening: use objective screening tools
    - When a family member or other informant is concerned
    - There are screening tools: e.g. Mini-Cog, General Practitioner Assessment of Cognition
2. Do further cognitive evaluation: Mini mental status examination

3. Evaluate for depression
4. Clinical evaluation and investigation for possible medical causes of dementia: HIV, hypothyroidism, vitamin B12 deficiency, review of medications.
5. Try to establish a specific cause for the dementia: see some of the clinical clues in the table below (table 11.3)
6. Brain imaging

Table 11.3: Clinical clues to common causes or mimickers of dementia

Adapted from: Am Fam Physician. 2018;97(6):398-405.

Cause	**Clinical clues**
Alzheimer disease	○ Insidious onset. No plateaus. ○ Recall of recent events is most affected ○ Apathy and sleep disturbances
Frontotemporal dementia	○ Socially inappropriate behaviors and compulsive behaviors ○ Loss of empathy ○ Significant in dressing or eating habits, religious or political beliefs ○ Progressive aphasia
Normal-pressure hydrocephalus	○ Urinary incontinence ○ Broad-based, shuffling gait
Vascular dementia	○ History of cerebrovascular events ○ Cardiovascular risk factors: hypertension, DM, smoking
Hypothyroidism	○ Fatigue, cold intolerance, constipation, weight gain, dry skin
VitaminB12 deficiency	○ Ascending paresthesias, limb weakness ○ Tongue soreness

Depression	○ Lack of interest in the environment, feelings of worthlessness, flat affect, sleep disturbance
Delirium	○ Recent hospitalization or acute illness ○ Fluctuating behavioral changes ○ Altered level of consciousness

TREATMENT

Objectives of treatment

- Correct reversible causes
- Improve functionality and quality of life
- Decrease caregiver's distress

Non pharmacologic

- Nutritional support: make sure patients get adequate nutrition and hydration
- Avoidance of alcohol
- Encourage exercise
- Address safety and legal issue: capacity to drive, legally and financial competency, ability to live alone or not

PHARMACOLOGIC TREATMENT

- Treatment for Alzheimer's diseases (mild to moderate): Cholinesterase inhibitors
  - **Donepezil**: starting dose 5mg, PO, once per day. Increase to 10mg once per/day in 1 – 2 months. Maximum dose 23mg/day
- Treatment of Lewy body, Parkinson's disease and vascular dementia: cholinesterase inhibitor may be considered in early stages (see Donepezil above)

- Treatment of severe behavioral (psychiatric) symptoms: aggression and agitation
    - **Citalopram**: Starting dose 20mg, PO, once per day. Increase to 30mg once per day in a week
- Psychotic symptoms which are refractory, disabling, and/or threatening patient or caregiver safety:
    - **Risperidone:** 0.5 to 1mg, PO, once per day.

REFERRAL

- If the service is not available patients with dementia should be referred for neurologist and psychiatrist evaluation and treatment after exclusion or treatment of reversible medical causes.

FURTHER READING

1. Nathan Falk, Ariel Cole, T. Jason Meredith. Evaluation of Suspected Dementia. Am Fam Physician. 2018;97(6):398-405

2. Daniela C. Moga , Monica Roberts, Gregory Jicha. Dementia for the Primary Care Provider. Prim Care Clin Office Pract 44 (2017) 439–456

3. Tony Foley, Aisling Jennings, Greg Swanwick. Dementia: Diagnosis & Management in General Practice Quick Reference Guide.

11.2 HEADACHE

BRIEF DESCRIPTION

- Headache is among the most common complaints that make patients seek medical attention.
- A large segment of the population suffers from headaches; resulting in a large number of over-the-counter medication use, work absenteeism, and significant economic impact.
- Although the most common causes of headache are benign, headaches

could also be presenting complaints of serious life-threatening diseases e.g., subarachnoid hemorrhage, meningitis, brain tumor

- Headaches are classified in to primary and secondary. Primary headaches are generally recurrent or chronic, no systemic or intracranial pathology can be identified. Secondary headaches result from identifiable systemic or intracranial disease.
- The commonest primary headache subtypes are migraine, tension type and cluster headache.
- The commonest causes of secondary headache can be memorized as "VOMIT":
    - **V**ascular: Intracranial hemorrhage: subdural, subarachnoid or intracranial hemorrhage
    - **O**ther causes: malignant hypertension, pseudotumor cerebri, post-lumbar puncture
    - **M**edication/drug related: alcohol withdrawal, chronic analgesic use/abuse
    - **I**nfection: meningitis, sinusitis, brain abscess
    - **T**umor
- The international headache society provides an extensive classification of headache. However, the entire document is not intended to be learned by heart. It can be referred when the diagnosis is in doubt.

CLINICAL EVALUATION OF HEADACHE

- The diagnosis of the specific cause of headache is made clinical; hence, a thorough history and examination is needed.

Table 11.4: History and physical examination in the evaluation of headache

Important elements of the headache history	**Physical examination**
o Onset e.g., very sudden (thunderclap) o Severity, progression and duration of attacks o Previous attacks o Pain location: unilateral, bilateral, neck pain o Associated symptoms – Nausea/vomiting – Photophobia – Rhinorrhea – Fever – Decreased vision, Conjunctival injection o Precipitating factors – Stress – Posture – Cough, Exertion and straining o Days per month with headache o Effect on quality of life: work and family o Response to medication o Amount of medication used o Coexistent conditions: depression, anxiety	o Vital signs: BP, temperature o Eye examination o Screening neurologic examination – Mental status – Cranial nerve examination and fundoscopy – Assessment of unilateral limb weakness, reflexes – Meningeal signs o Neck examination: posture, range of motion, and palpation for muscle tender points

Table 11.5: Red flag features (danger signs and symptoms) in a patient with headache

No	Danger sign or symptom	Possible diagnoses	Investigations
1	The worst headache ever	Subarachnoid hemorrhage	Brain imaging, LP
2	Sudden onset (maximal intensity within seconds to minutes)	Subarachnoid hemorrhage Bleeding into a mass	Brain imaging and LP
3	Headache following trauma	Intracranial bleeding	Brain imaging
4	Triggered by: cough, exertion or sexual intercourse	Subarachnoid hemorrhage Mass lesion	Brain imaging, LP
5	New onset headache after the age of 50	Mass lesion	Brain imaging
6	New onset of severe headache in pregnancy or postpartum	Cerebral sinus thrombosis	Brain imaging
7	New onset headache with progressively worsening pattern	Subdural hematoma, Intracranial space occupying lesion (tumor, abscess, bleeding)	Brain imaging
8	Decreased vision, conjunctival redness, eye pain	Acute glaucoma	
9	Focal neurologic signs	Intracranial space occupying lesion (tumor, abscess, bleeding)	Brain imaging
10	Headache with behavioral or mental status changes	CNS infection, mass lesion	Brain imaging, LP

11	Neck stiffness or meningismus	Meningitis, Subarachnoid hemorrhage	Lumbar puncture
12	Fever and systemic symptoms with headache	Meningitis, Malaria, Typhoid Fever, Connective tissue diseases	Blood tests, LP
13	New headache in a patient with HIV	Opportunistic CNS infections or tumor (Cryptococcal meningitis, CNS toxoplasmosis, tuberculosis, CNS lymphoma)	Brain imaging, LP
14	New onset headache in a patient with Cancer	Metastasis	Lumbar puncture, neuroimaging

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of the cause of headache is mainly clinical
- Patients suspected of having secondary headache or having red flag features need further investigation (brain imaging, LP or blood tests according to the suspected diagnosis)

TREATMENT

- The treatment of primary headaches (see the treatment section of primary headaches in the next sessions)
  - Establish the primary headache syndrome
  - Assess the impact on quality of life
  - Focus on preventive therapy than frequent symptomatic therapy
- The treatment of secondary headaches: identify and treat the cause accordingly

FURTHER READING

1. Werner J. Becker, Ted Findlay, Carmen Moga et al. Guideline for primary care management of headache in adults. Can Fam Physician 2015; 61:670-9
2. Barry L. Hainer and Eric M. Matheson. Approach to acute headache in adults. Am Fam Physician. 2013;87(10):682-687
3. International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018; 38:1–211

11.2.1 MIGRAINE HEADACHE

BRIEF DESCRIPTION

- Migraine headache is an inherited disorder (probably an autosomal dominant trait with incomplete penetrance).
- Migraine is more prevalent among women and is strongly influenced by hormonal cycles.

- It is also more common in those with a family history.
- There are several recognized subtypes of migraine: hemiplegic migraine, retinal migraine, vestibular migraine, migraine with brain stem aura, menstrual migraine, and chronic migraine
- Complications of migraine: prolonged/refractory headache, infarction, and seizure.
- Status migrainosus is defined as a migraine headache that lasts over 72 hours.

CLINICAL FEATURES

- **Prodromal phase** (occurs in 30% of patients)
    - Occur 24 to 48 hours prior to the onset of headache
    - Frequent yawning
    - Mood changes: euphoria, irritability, depression, irritability
    - Food cravings: craving for certain foods (especially sweets)
- **Migraine aura**
    - About 25-30% experience neurologic symptoms before or at the onset of headache , called the migraine aura
    - Aura develop gradually over few minutes to an hour
    - The commonest aura is visual
        - Flashes of light, bright lines, shapes or objects.
        - Visual effects grow or move across.
    - Other types of auras
        - Auditory: noises, music, tinnitus, decreased hearing
        - Sensory: pain, paresthesia, burning sensation, loss of sensation
        - Motor: jerking or repetitive rhythmic movements or transient paralysis

        - Negative visual: loss of vision

- **The migraine headache**
    - Usually severe and throbbing. It can also be dull and achy.
    - Usually unilateral but not always on the same side, it can be bilateral.
    - Lasts few hours to days
    - Associated symptoms:
        - Nausea and vomiting (~90% of cases)
        - Photophobia and/or phonophobia: seeking quiet and dark room to rest
        - Increased sensitivity to smell
    - Triggers/precipitants: Emotional stress, menstrual cycle, not eating, weather, sleep disturbance, odors, lights, alcohol, certain food items and physical activity
- **Postdrome**
    - Head movement may cause pain in the side which had headache.
    - Feeling drained or exhausted

INVESTIGATION AND DIAGNOSIS

- The diagnosis of migraine headache is clinical.
- Further investigation will be needed if secondary causes are suspected (see the general headache section)
- The International headache classification criteria can be used to assist in the diagnosis (see the table 11.6 below)

TREATMENT

OBJECTIVES OF TREATMENT

- Decrease recurrence and reduce the need for analgesia
- Improve quality of life

- Relive headache effectively

NONPHARMACOLOGICAL

- Identification and management of migraine triggers
- A headache diary: document the number and severity of headaches each month and identified precipitating factors
- Lifestyle measures: good sleep hygiene, routine meal schedules, and regular exercise.

Table 11.6: Diagnostic criteria for Migraine with or without aura

Migraine without aura	Migraine with aura
A. At least 5 attacks fulfilling criteria B–D	**A**. At least 2 attacks fulfilling criteria B & C
B. Headache attacks lasting 4–72 h (untreated or unsuccessfully treated)	**B**. One or more of the following fully reversible aura symptoms: Visual, Sensor, Speech and or language, motor, Brainstem, Retinal
C. Headache has at least two of the following four characteristics: 1. Unilateral location 2. Pulsating quality 3. Moderate or severe pain intensity 4. Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)	**C**. At least two of the following four characteristics: 1. At least one aura symptom spreads gradually over ≥5 min 2. Two or more aura symptoms occur in succession 3. Each individual aura symptom lasts 5–60 min 4. At least one aura symptom is unilateral 5. At least one aura symptom is positive 6. The aura is accompanied, or followed within 60 min, by headache
D. During headache at least one of the following: 1. Nausea and/or vomiting 2. Photophobia and phonophobia	**D.** Not better accounted for by another diagnosis
E. Not better accounted for by another diagnosis	

Ref: Cephalalgia 2018; 38:1–211

PHARMACOLOGIC TREATMENT

- The pharmacologic treatment of migraine is classified in to two: treatment of acute attacks abortive therapy) and preventive (prophylactic therapy)

TREATMENT OF ACUTE ATTACKS OF MIGRAINE (ABORTIVE THERAPY)

- Effective if given early at the onset
- Use larger doses once than repetitive small doses
  - o Mild to moderate Migraine without nausea and vomiting: Options
    - **Paracetamol** 1 gm PO once
    - **Ibuprofen** 400 mg PO once
    - **Diclofenac** 50 -75 mg PO or IM once
    - **Aspirin** 1000mg PO once
  - o Moderate to severe attack without nausea and vomiting
    - Sumatriptan 6 mg subcutaneous injection
    - If subcutaneous formulation is not available: Sumatriptan 50 mg to 100 mg PO once.
  - o Moderate to severe attack with vomiting
    - Sumatriptan 6 mg subcutaneous injection PLUS Metoclopramide 10 mg IV stat
  - o Status migrainosus
    - As in severe migraine PLUS Dexamethasone 4 mg IV/IM to prevent relapse
- NSAIDs are effective for menstrual migraines

PROPHYLAXIS (PREVENTIVE THERAPY)

- Indications for prophylactic therapy
    - Frequent (e.g., weekly) or long-lasting migraine headaches interfering with activity
    - Migraine attacks that cause significant disability or diminished quality of life
    - Problem with acute therapy: contraindication, serious adverse effects, failure
    - Risk of medication overuse headache
    - Menstrual migraine
- Consideration during prophylactic therapy
    - Educate patients on the need to take the medication daily
    - Start low dose and increase until effective dose or maximum dose is achieved
    - Continue the prophylactic drug for at least 6-8 wk after dose titration before regarding it as ineffective.
    - Realistic expectations as:
        - It might take 4-8 wk for benefit to occur
        - A reduction in headache frequency of at least by 50% is considered successful
    - Discontinuation can be considered after 12 months of successful prophylactic therapy
- First-line agents for prophylaxis:
    - A beta blocker or a tricyclic antidepressant
    - Start either of them and escalate the dose. If maximum tolerated dose of beta-blocker fails shift to antidepressant and vice-versa.

Table 11.7: First line agents for migraine prophylaxis

Beta blockers		
	Starting dose	**Dose range**
Propranolol	40mg/day in two divided doses	40 -160mg/day
Atenolol	25mg/day	25 -100mg/day
Metoprolol	50mg/day	50 -200mg/day
Tricyclic antidepressant		
Amitriptyline	12.5mg/day	12.5 – 50mg/day

- Second line prophylactic agents
    - **Sodium Valproate**: starting dose 500mg/day (in two divided doses for immediate release or single dose for extended release). Usual dose range 500-1500mg/day
    - **Verapamil**: starting dose 120/day (in three divided doses). Usual dose range 240/day.
- Consideration of medication overuse headache (see this topic in this guideline)
    - Patients who frequently use acute pain reliving medications are at high risk
    - These occur more frequently (every 1 to 2 days) than migraines.
    - These headaches do not respond to drugs used to treat migraines.

FURTHER READING

1. Rebecca Burch. Migraine and Tension-Type Headache: Diagnosis and Treatment. Med Clin N Am (2018) .https://doi.org/10.1016/j.mcna.2018.10. medical.theclinics.com
2. Werner J. Becker, Ted Findlay, Carmen Moga et al. Guideline for primary care management of headache in adults. Can Fam Physician 2015; 61:670-9

3. Azmin Kahriman, Shuhan. Migraine and Tension-Type Headache. Semin Neurol 2018; 38:608–618.
4. The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018; 38:1–211

11.2.2 TENSION TYPE HEADACHE

BRIEF DESCRIPTION

- Tension type headache is the most common head ache in the general population.
- Tension type headache frequently often coexists with migraine, and differentiating the two could be challenging.
- Tension type headache is less likely to cause severe pain and functional impairment.
- It usually presents as bilateral pain of pressing or tightening quality, in contrast to unilateral pulsating pain of the migraine.
- Most individuals affected by infrequent episodes do not seek medical attention.
- Based on the frequency it is divided in to three (see diagnosis below)
    - Infrequent episodic
    - Frequent episodic
    - Chronic

CLINICAL FEATURES

- The headache starts at some point during the day and commonly persists in the reminder of the day with possible aggravation toward the end of the day.
- Pain is steady, aching and encircles the entire head (tight band-like pain around the head).

  - Usually generalized, but may more intense around the neck or back of head.
  - Can be accompanied by tender muscles (posterior cervical, temporal, frontal)
  - Tightness in posterior neck muscles.

INVESTIGATION AND DIAGNOSIS

- The diagnosis of tension type head is clinical.
- Further investigation will be needed if secondary causes are suspected (see the general headache section)
- The International headache classification criteria can be used to assist in the diagnosis and classification of tension type headache (see table 11.8 below)

Table 11.8: ICHD-3 diagnostic criteria for Tension type headach

Infrequent or frequent tension type headache - Infrequent: <1 day/month on average. - Frequent : 1–14 days/month on average for >3 month	**Chronic tension type headache**
A. At least 10 episodes of headache fulfilling criteria B–D	A. Headache occurring on≥15 days/month on average for >3 month(≥180 days/year), fulfilling criteria B–D
B. Lasting from 30 min to 7 days	B. Lasting hours to days, or unremitting

C.At least two of the following four characteristics 1. Bilateral location 2. Pressing or tightening (non-pulsatile) quality 3. Mild or moderate pain intensity 4. Not aggravated routing physical activity such as walking or climbing stairs	C. At least two of the following four characteristics 1. Bilateral location 2. Pressing or tightening (non-pulsatile) quality 3. Mild or moderate pain intensity 4. Not aggravated routing physical activity such as walking or climbing stairs
D. Both of the following 1. No nausea and/or vomiting 2. No more than one of photophobia, phonophobia,	D. Both of the following 1. No more than one of photophobia or phonophobia 2. Neither moderate or severe nausea nor vomiting
E. Not better accounted for by another ICHD-3 diagnosis	E. Not better accounted for by another diagnosis

Ref: Cephalalgia 2018;38:1–211

TREATMENT

OBJECTIVES OF TREATMENT

- Relive symptoms
- Reduce frequency of headache
- Reduction medication overuse headache

Non pharmacologic

- Evaluate the patient for possible depression or anxiety.
- Identification of headache triggers and correction of behavior: triggers are similar to migraine

- A headache diary is helpful to identify frequency, severity and triggers

PHARMACOLOGIC

- **Acute treatment**
    - First line: NSAIDS or Paracetamol
        - **Paracetamol** 1 gm PO once
        - **Ibuprofen** 400 mg PO once
        - **Diclofenac** 50 -75 mg PO or IM once
        - **Aspirin** 1000mg PO once
    - If headaches are severe, medications that are used for migraines (Sumatriptan) may be appropriate, given the difficulty in distinguishing between these two entities.
- **Prophylactic therapy**
    - Patients with infrequent tension type headaches do not need pharmacologic prophylaxis
    - Indications for pharmacologic prophylactic therapy
        - Chronic tension type headache (see diagnostic criteria above)
        - Frequent tension type headache: causing significant disability
    - Prophylactic agent
        - Amitriptyline: Starting dose 12.5 to 25mg at bed time. Usual dose 25 -100mg/day.

FURTHER READING

1. Rebecca Burch. Migraine and Tension-Type Headache: Diagnosis and Treatment. Med Clin N Am (2018) .https://doi.org/10.1016/j.mcna.2018.10. medical.theclinics.com
2. Werner J. Becker, Ted Findlay, Carmen Moga et al. Guideline for primary care management of headache in adults. Can Fam Physician 2015;61:670-9

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4. The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38:1–211

11.2.3 MEDICATION OVERUSE HEADACHE

BRIEF DESCRIPTION

- Medication overuse headache refers to headache that results from frequent use of acute pain-relieving medication for other primary headache (usually migraine or tension type headache
- Although there is no specific threshold, use of NASAIDs or paracetamol for more than 15days per month and use of triptans, ergots or caffeine containing analgesics for more than 10days per month should be avoided.

CLINICAL FEATURES

- Features of the primary headache: Medication overuse headache preceded by primary headache syndrome
- Usually present or develops upon awakening
- Daily or nearly daily
- Other associated features
    - Nausea, fatigue
    - Difficulty concentrating
    - Memory problems
    - Irritability

INVESTIGATION AND DIAGNOSIS

- The diagnosis of medication overuse headache is clinical.
- The course of the headache disorder, the frequency of drug intake are the only available methods of diagnosis

- The diagnostic criteria medication overuse headache requires fulfillment of the following three criteria:

1. Headache occurring on 15 or more days per month in a patient with a pre-existing headache disorder
2. Regular overuse for more than three months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache:
   - Regular intake, for ≥10 days per month for >3 months: for ergotamine, triptans, opioids, or combination
   - Regular intake, for ≥15 days per month for >3 months, of simple analgesics : paracetamol or NSAIDS
3. Not better accounted for by another diagnosis

TREATMENT

OBJECTIVES OF TREATMENT

- Enable reduction or stopping the overused medication
- Improve functionality and quality of life

PRINCIPLES OF TREATMENT

- Patient education
- Discontinuation of the offending medication
- Offer rescue abortive: no more than two days per week, from a different class
- Bridge (transitional) therapy
  - High dose steroid for 2-3 days as bridge therapy
    - **Prednisolone** 100mg/day x 2-3days
    - **Dexamethasone** 12 – 16mg, IM/day 2-3 days
- Providing appropriate prophylactic therapy for the primary headache
- Follow up

REFERRAL

- Difficulty in stopping medications warrants a referral to a neurologist or psychiatrist.

FURTHER READING

1. Wakerley BR. Medication overuse headache. Pract Neurol 2019;0:1–5.
2. Ann I. Scher, Paul B. Rizzoli, Elizabeth W. Loder. Neurology Sep 2017, 89 (12) 1296-1304

11.2.4 CLUSTER HEADACHES

BRIEF DESCRIPTION

- Cluster headache is a trigeminal autonomic cephalalgia characterized by extremely painful, strictly unilateral, short-lasting headache attacks accompanied by ipsilateral autonomic symptoms or the sense of restlessness and agitation, or both.
- The headache is so severe that the patient's quality of life is significantly affected, in some cases, might lead to suicidal ideation.
- Common subtypes include
  1. Episodic cluster headaches (90% of cases)
  2. Chronic cluster headaches (10% of cases)
- Cluster headache is uncommon but debilitating

CLINICAL FEATURES

- Excruciating periorbital pain ("behind the eye"): **almost always unilateral.**
- Cluster headache is described as a "deep, burning, searing, or stabbing pain." Pain may be so severe that the patient may even become suicidal.
- Accompanied by ipsilateral lacrimation, facial flushing, nasal stuffiness/discharge

- Usually begins a few hours after the patient goes to bed and lasts for 30 to 90 minutes; awakens patient from sleep (but daytime cluster headaches can also occur).
- Attacks occur nightly for 2 to 3 months and then disappear. Remissions may last from several months to several years.
- Worse with alcohol and sleep.

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of cluster headache is clinical
- The ICHD-3 diagnostic criteria is useful to confirm the diagnosis

Table 11.9: ICHD-3 diagnostic criteria for cluster headache

It requires all of the followings

1. At least five attacks
2. Attacks characterized by severe or very severe unilateral orbital, supra-orbital and/or temporal pain lasting 15 - 180 minutes when untreated.
    - Less than half of the times cluster headache attacks may be less severe and/or of shorter or longer duration.
3. Either or both of the following:
    - At least one of the following symptoms or signs ipsilateral to the headache:
        - Conjunctival injection and/or lacrimation
        - Nasal congestion and/or rhinorrhea
        - Eyelid edema
        - Forehead and facial sweating
        - Forehead and facial flushing
        - Sensation of fullness in the ear
        - Miosis and/or ptosis
    - A sense of restlessness or agitation
4. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active
5. Not better accounted for by another ICHD-3 diagnosis

Diagnostic criteria for **episodic** cluster headache require the following:

1. Attacks fulfilling criteria for cluster headache and occurring in bouts (cluster periods)
2. At least two cluster periods lasting from seven days to one year (when untreated) and separated by pain-free remission periods of one month or more

Diagnostic criteria for **chronic** cluster headache require the following :

1. Attacks fulfilling criteria for cluster headache
2. Attacks occurring without a remission period, or with remissions lasting less than one month, for at least one year

TREATMENT

OBJECTIVES OF TREATMENT

- Relive acute pain
- Decrease recurrence

Pharmacologic

- **Acute attacks: 100% oxygen or sumatriptan**
  - Oxygen (100 percent)
    - Via a non-rebreathing facial mask
    - Flow rate: at least 12 L/min (up to 15L/min)
    - Position: sitting, upright position
    - Duration: 15 minutes even if the pain subsides early

    OR

  - Sumatriptan: 6 mg subcutaneous injection, maximum of two doses in 24 hours
- **Prophylaxis**
  - For patients with chronic cluster headache and those with two months or longer lasting episodic cluster headaches:

- **Verapamil**:
    - ✓ Starting dose 240 mg in three divided doses.
    - ✓ Usual dose 240 - 320 mg /day.
    - ✓ Maximum dose 960 mg/day
    - ✓ Close monitoring for bradycardia and low blood pressure.

○ For those with episodic cluster headache that last less than two months

- **Prednisolone**
    - ✓ 60 -100 mg once a day for seven days
    - ✓ Taper: reduce 10 mg daily.

FURTHER READING

1. Matthew S. Robbins, Amaal J. Starling, Tamara M. Pringsheim et al. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache 2016; 56:1093-1106.
2. Jan Hoffmann, Arne May. Diagnosis, pathophysiology, and management of cluster headache. www.thelancet.com/neurology Published online November 23, 2017 http://dx.doi.org/10.1016/S1474-4422(17)30405-2

11.3 MOVEMENT DISORDERS

11.3.1 OVERVIEW OF MOVEMENT DISORDERS

- Movement disorders are a variable group of neurologic disorders common in primary care practice.
- The clinical presentation of some movement disorders can be fairly straight forward while some movement disorders are complex, often variable, and sometimes even bizarre.
- Movement disorders can be primary (the disorder being the primary

neurologic disease without any other pathology) or secondary.

- Movement disorders are broadly classified in to two

1) **Hyperkinetic movement disorders**: refers to excessive, often repetitive, involuntary movements that intrude into the normal flow of motor activity.
    - Tremor
    - Chorea
    - Dystonia
    - Myoclonus
    - Tics

1) **Hypokinetic movement disorders:** refers to akinesia (lack of movement), hypokinesia (reduced amplitude of movement), bradykinesia (slow movement), and rigidity.
    - Parkinsonism is the primary hypokinetic movement disorder.

- Definition and description of hyperkinetic movement disorders
    - **Myoclonus**: sudden, brief, shock-like involuntary movements, usually caused by muscle contraction but can sometimes be due inhibition of muscle tone.
    - **Chorea:** involuntary movements which are abrupt, unpredictable and non-rhythmic; best described as "randomly flowing jerks"
    - **Ballismus**: ballistic movements are uncontrollable, severe, mainly proximal, large-amplitude chorea movement. Usually unilateral (hemiballismus)
    - **Tremor**: involuntary, rhythmic and alternating movements of one or more body parts.

Tremor can affect almost any body part, commonly the limbs, head and neck, soft palate

The keyword in identifying tremor is 'rhythmicity'

- **Dystonia**: an involuntary abnormal co-contraction of antagonistic muscles resulting in abnormal characteristic postures and movements, which distort limbs, the trunk, neck, face or mouth.
- **Tics**: repeated, individually recognizable, intermittent movements or movement fragments that are almost always briefly suppressible and are usually associated with awareness of an urge to perform the movement.
  - **Characteristic** features include predictability and brief(temporary) voluntary suppressibility
- **Stereotypies:** repetitive, simple movements that can be voluntarily suppressed.

Table 11.10: Classification of tremor

Type of tremor	Description	Exampleof underlying cause
1. **Rest tremor**	Occurs in a body part that is relaxed and completely supported against gravity	Parkinsonism
2. **Action**	Occurs with activity (voluntary contraction of muscle)	
• Postural	Occurs in body part that assumes a posture against gravity	Essential tremor Physiologic tremor Drug-induced tremors
• Simple kinetic	Occurs during entire movement trajectory	Essential tremor
• Intention	Subtype of kinetic tremor amplified as the target is reached	Cerebellar
• Task specific	Occurs only during specific activities	Dystonic writing tremor

Enhanced physiologic tremor: physiologic tremor is present in all persons. This tremor can be enhanced by anxiety, stress, and certain medications or metabolic conditions. It does not need further investigation or treatment.

- Medications associated with tremor: there are a number of medications that are associated with tremor.
- Some common drugs associated with tremor

– Beta-adrenergic agonists (e.g., salbutamol)	– Caffeine
– Carbamazepine	– Corticosteroids
– Haloperidol	– Metoclopramide
– Pseudoephedrine (found in cough syrups)	– Theophylline
– Thyroxine	– Tricyclic antidepressants

FURTHER READING

1. Wilson F.Abdo, Bart P. C. van de Warrenburg, David J. Burn et.al.The clinical approach to movement disorders. Nat. Rev. Neurol. 6, 29–37 (2010); doi:10.1038/nrneurol.2009.196
2. Paul Crawford and Ethan E. Zimmerman. Differentiation and Diagnosis of Tremor. Am Fam Physician. 2011;83(6):697-702.

11.3.2 ESSENTIAL TREMOR

BRIEF DESCRIPTION

- It is considered to be the most common pathologic tremor.
- About half of the cases are familial, in an autosomal dominant inheritance fashion
- It usually starts in early adulthood but most patients do not seek help until late in their life because of the progressive nature of the tremor

- It can cause significant social embarrassment, earlier retirement or change in carrier.
- There is no known association between essential tremor and Parkinson disease.

CLINICAL FEATURES

- Essential tremor is an action tremor: usually postural and/or kinetic.
- It is most obvious in the wrists and hands when patients hold their arms in front of themselves (resisting gravity); however, essential tremor can also affect the head, and voice.
- Lower limb is rarely involved. Lower limb involvement with rigidity should suggest Parkinson's tremor.
- It is also commonly noticeable while performing tasks such as drinking from a cup, writing, or reaching for an object. Distorted handwriting is often present.
- It is generally symmetric but can sometimes be asymmetric(unilateral).
- Tremor markedly decreases by alcohol use
- It usually remains mild and stable for many years but can slowly worsen over time.

INVESTIGATION AND DIAGNOSIS

- The diagnosis is clinical. The primary criteria is the presence of either of the following:
  1. Bilateral action tremor of the hands and forearms (but not resting tremor) in the absence of other neurologic signs with the exception of cogwheel phenomenon
  2. Isolated head tremor with no features of dystonia
- Supportive diagnostic criteria. The presence of one or more of the following supports the diagnosis
  1. Long duration > 3 years

2. Positive family history
3. Beneficial response to alcohol

TREATMENT

OBJECTIVES OF TREATMENT

- Improve functionality

Non-pharmacologic

- Decrease stress
- Minimize caffeine intake

Pharmacologic

- Drug treatment should only be offered to those with intermittent or persistent disability caused by the tremor
- First line
  - **Beta blocker:** Propranolol is preferred due to more evidences but other beta blockers could be used
    - **Propranolol**

      Starting dose 40m BID.

      Usual maintenance doses 120 to 320 mg/day 2 to 3 divided doses

REFERRAL

- Patients who have essential tremor causing significant disability and not responding to propranolol should be referred to a referral hospital with neurologic services.

FURTHER READING

1. Benito-León, J., & Louis, E. D. (2006). *Essential tremor: emerging views of a common disorder. Nature Clinical Practice Neurology, 2(12), 666–678.* doi:10.1038/ncpneuro0347
2. Sharma S, Pandey S. Treatment of essential tremor: current status Postgrad Med J 2019;0:1–10. doi:10.1136/postgradmedj-2019-136647

11.3.3 PARKINSON DISEASE

BRIEF DESCRIPTION

- Parkinson disease is the most common cause of hypokinetic movement disorder.
- Parkinson disease is a progressive neurodegenerative syndrome involving multiple motor and non-motor neural circuits.
- Although rare forms can occur at younger age, the most important risk factor for Parkinson's disease is old age.
- Onset is usually after age 50 years.
- The diagnosis of Parkinson disease is essentially clinical. Laboratory studies play no role in diagnosis.

CLINICAL FEATURES

- The cardinal features of Parkinson's disease: Tremor, Rigidity, Akinesis/ bradykinesia, +/- Postural instability. Remembered by the mnemonic **TRAP.**
- **Tremor**
  - Resting tremor: noticeable when the tremulous part is supported. Tremor is usually noticed when the arm is passively resting on the lap of the patient.
  - Described as "pill-rolling"
  - Intermittent: may not be noticeable during examination
  - Starts unilaterally in the arm: takes years before it progresses to the contralateral side
  - The legs, lips, jaw, and tongue can be involved. Head involvement is not characteristic,
- **Bradykinesia** (slowness of movement)
  - Present in most patients starting from the onset

  - Difficult symptom for patients to describe.
  - Patients may describe it as: "Weakness," "incoordination," and "tiredness"
  - Decreased manual dexterity of the fingers: unable to do buttoning of clothes, tying shoelaces,
  - Dragging the legs, shorter (shuffling) step and unsteadiness
  - Gait freezing
  - Festination: an impulse to take quicker and shorter steps, resulting in an unwanted running pace
- **Rigidity**
  - Rigidity is an increased resistance to passive movement about a joint
  - Decreased arm swing with walking
- **Postural instability**
  - Appears very late in the course
  - A feeling of imbalance and a tendency to fall with a significant risk of injury.
- **Other motor features**
  - Masked facial expression, dysarthria, hypophonia, and palilalia (repetition of a phrase or word with increasing rapidity), dysphagia
  - Micrographia
  - Stooped posture, kyphosis, scoliosis
  - Difficulty turning in bed
- **Non-motor features**
  - Cognitive dysfunction and dementia
  - Psychosis and hallucinations
  - Mood disorders: depression, anxiety, and apathy

  - Sleep disturbances
  - Autonomic dysfunction: postural dizziness, constipation, urinary difficulties
- **Progressive course**

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of Parkinson disease is clinical.
- The diagnosis depends on the presence of the cardinal features: bradykinesia, rigidity, tremor, and postural instability
- The gradual progression and sustained response to therapy with levodopa support the diagnosis
- Conditions that mimic Parkinson disease. Some clinical clues help in differentiating them

  1. Vascular parkinsonism
     - Due to basal ganglia or thalamic ischemia (ischemic stroke).
     - Focal neurologic findings may be present.
  2. Drug induced parkinsonism: antipsychotic and antiemetics
  3. Dementia with Lewy bodies
     - Onset of the motor symptoms accompanied by dementia and visual hallucinations.
     - Marked fluctuations in attention and cognition.
  4. Atypical parkinsonism (supranuclear palsy and multisystem atrophy):
     - Similar to Parkinson disease, but other motor signs appear very early in the diseases
     - Early development of prominent gait and speech impairment, prominent postural instability and autonomic dysfunction.
     - Typical resting tremor usually lacking

TREATMENT

OBJECTIVES OF TREATMENT

- Improve functionality and quality of life
- Decrease medication adverse effects

Non-pharmacologic

- Patient and family education

Pharmacologic treatment

- **First line: Levodopa based therapy**
    - **Carbidopa-levodopa** (10/100, 25/100, and 25/250 mg)
        - Dosing for 25/100 mg tablet:

One-half tablet, TID, with meals.

Gradually titrate over several weeks to a full tablet, TID.

- Dosing for 25/250mg

One-half tablet, BID, with meals.

- Gradually titrate over several weeks to a full tablet BID to TID
- Maintain the lowest effective dose.
- Levodopa should not be stopped abruptly
- Nausea is a common side effect but metoclopramide should be avoided as it can aggravate parkinsonian symptom

- **Anticholinergic drugs**
    - Indications
        1. As a monotherapy: for patients who are **<70 years** and have disturbing tremor (tremor predominant disease) without significant bradykinesia or gait disturbance.

2. As an add-on to levodopa: in patients with more advanced disease with persistent tremor despite treatment with levodopa.

- o Medication: Trihexyphenidyl
    - Starting dose 0.5 to 1 mg BID
    - Gradually increase to 2 mg TID.

REFERRAL

- Most patients with Parkinson disease need follow up by neurologist. If there are significant symptoms despite optimal levodopa therapy or failure to tolerate levodopa, refer to a referral hospital with neurology service.

FURTHER READING

1. John D. Gazewood, D. Roxanne Richards, Karl Clebak. Parkinson Disease: An Update. Am Fam Physician. 2013;87(4):267-273
2. R. Balestrino and A.H.V. Schapira. Parkinson disease. European Journal of Neurology 2020, 27: 27–42.
3. Philippe Rizek , Niraj Kumar , Mandar S. Jog. An update on the diagnosis and treatment of Parkinson disease. CMAJ, November 1, 2016, 188(16).

11.4 SEIZURE DISORDER AND EPILEPSY

BRIEF DESCRIPTION

- A seizure occurs when there is a sudden abnormal discharge of electrical activity in the brain.
- Seizures could be symptomatic to transient causes or due to epilepsy.
- Acute symptomatic seizure refers to a seizure that occurs at the time of a systemic insult or in close temporal association with a documented brain insult.
- Epilepsy refers to a syndrome of recurrent, idiopathic seizures.
- Pseudo seizures are not true seizures but are psychiatric in origin and

often difficult to distinguish from true seizures without an EEG.

- Causes of seizures can be remembered by the four M's and the four I's
- The four M's

1. **M**etabolic and electrolyte disturbances: hyponatremia, hypoglycemia or hyperglycemia, hypocalcemia, uremia, thyroid storm, hyperthermia.
2. **M**ass lesions: brain metastases, primary brain tumors, hemorrhage.
3. **M**issing drugs (Noncompliance) with anticonvulsants in patients with epilepsy. This is the most common reason for poor seizure control in epileptics.
4. **M**iscellaneous
   - o Eclampsia
   - o Hypertensive encephalopathy: severe hypertension can cause cerebral edema.
   - o Acute withdrawal from alcohol, benzodiazepines, barbiturates.

- The four I's

1. **I**ntoxications: cocaine, lithium, theophylline, carbon monoxide poisoning.
2. **I**nfections: malaria, bacterial or viral meningitis, brain abscess, sepsis.
3. **I**schemia: stroke, TIA (common cause of seizure in elderly patients).
4. **I**ncreased ICP: for example, due to trauma.

CLASSIFICATION OF EPILEPTIC SEIZURES

- The 2017 international league against epilepsy (ILAE) classification is based on 3 key features.
  - I. Where seizures begin in the brain? Focal, generalized or unknown
  - II. Level of awareness during a seizure? For focal aware or impaired awareness
  - III. Other features of seizures? Motor or non-motor. If motor either tonic-

clonic or other motor

- Defining where Seizures Begin
  I. **Focal onset seizures:** Previously called partial seizures
  II. **Generalized onset seizures:** Previously called primary generalized
  III. **Unknown onset:** If the onset of a seizure is not known

Table 11.11: ILAE 2017 classification of seizure types: basic version

First level Classification	**Second level** **Classification**	**Third level**	**Fourth level**
Focal onset	Aware or impaired awareness	Motor onset or non-motor onset	Focal to bilateral tonic-clonic
Generalized onset	Motor or Non-motor (absence)	If Motor: Tonic-clonic or Other motor	
Unknown onset	Motor or Non-motor (absence)	If Motor Tonic-clonic or Other motor	
Unclassified			

- **Focal onset seizure**
  - If the onset of the seizure is focal describe the awareness.
  - Awareness is used instead of consciousness, for classification because it is simpler to evaluate.
  - **Focal aware:** If awareness remains intact, even if the person is unable to talk or respond during a seizure, the seizure would be called a focal aware seizure. This replaces the term simple partial.
  - **Focal impaired awareness:** If awareness is impaired or affected at any time during a seizure, even if a person has a vague idea of what

happened, the seizure would be called focal impaired awareness. This replaces the term complex partial seizure.

  - **Awareness unknown:** the awareness term may not be used or it would be described as awareness unknown.
  - **Focal to bilateral seizure:** previously called secondary generalized seizure. Now the term generalized refers only to a generalized onset seizure.
  - **Focal motor seizure:** some type of movement occurs during the event (twitching, jerking, or stiffening or automatisms (licking lips, rubbing hands, walking, or running).
  - **Focal non-motor seizure**: This type of seizure has other symptoms that occur first, such as changes in sensation, emotions, thinking, or experiences.
- **Generalized seizures:** These are all presumed to affect a person's awareness or consciousness in some way. Thus no special terms are needed to describe awareness in generalized seizures.
  - **Generalized motor seizure**: describes tonic and clonic seizure.
  - **Generalized non-motor seizure:** These are primarily absence seizures.

DIAGNOSIS

- If the patient has a known seizure disorder (epileptic), check adherence.
- If the patient history is unclear or if this is the patient's first seizure:
  - CBC, electrolytes, blood glucose, LFTs, renal function tests, urinalysis.
  - EEG
    - Although the EEG is the most helpful diagnostic test in the diagnosis of a seizure disorder, an abnormal EEG pattern alone is not adequate for the diagnosis of seizures.
    - A normal EEG in a patient with a first seizure is associated with a lower risk of recurrence.

  - LP and blood cultures—if patient is febrile.

TREATMENT

NON PHARMACOLOGIC

- Patient and family education on epilepsy, adherence, risky activities, driving and emergency management
- Avoiding precipitants

PHARMACOLOGIC

General principles of pharmacologic therapy

- Indication to start antiepileptic drug therapy after first unprovoked seizure and
- All non-symptomatic seizures two or more episodes
  - Epileptiform abnormalities on interictal electroencephalogram (EEG)
  - Remote cause: identified by history or neuroimaging (e. g brain tumor, brain malformation, prior central nervous system infection)
  - Abnormal neurologic examination
  - A first seizure that occurs during sleep
- Patients with a history of seizures (epilepsy)
  - Start treatment with one antiepileptic drug
  - If seizures persist, increase the dosage of the first anticonvulsant until signs of toxicity appear.
  - Add a second drug if the seizures cannot be controlled with the drug of first choice.
  - If the patient remains seizure free, decrease the dose of the medication(s) cautiously.
  - Discontinuation of antiepileptic drugs can be considered if a patient has been completely free of seizures for at least two year; however, risk of recurrence of seizures should be discussed with the patient.

- The decision of discontinuation should be individualized as the risk of recurrence is variable and it should be made by a specialist.

- Antiepileptic drug choices by seizure types (see table below)
- Antiepileptic drug dosing and titration (see table below)

Table 11.12. Common antiepileptic drug choices for adults by seizure type

Seizure type	First line options	Alternatives (second line)
Focal onset Seizure	Carbamazepine	Valproic acid
	Phenytoin	Phenobarbital
Generalized onset: Motor	Valproic acid	
	Phenobarbital	
	Carbamazepine	
	Phenytoin	
Absence	Valproic acid	Phenobarbital, phenytoin,
		Carbamazepine

Table 11.13. Common antiepileptic drug dosing

Drug	Initial dosage	Maximum dosage: not necessarily required	Titration and administration
Carbamazepine	100–200mg BID	2,400 mg daily (usual effective dose 400 -1200mg/day)	- Increase 200 mg/day - extended release in 2 divided doses - Regular formulation: 2–4 divided doses for

Phenobarbital	30–100mg daily	300 mg daily (usual effective dose 60-200mg)	- Titrate in 30 mg increments per 1–2 weeks - As it is sedating, give at bedtime - If morning sedation occurs divide in to 2 doses.
Phenytoin	100mg TID	600 mg daily (usual effective dose ~300mg/day)	- Doses up to 200 mg 3 times a day may be necessary. - Consider converting patients from TID doses to BID and once daily doses after good seizure control
Valproic acid	500mg daily: extended release 250mg BID: delayed release	3,000 mg (usual effective dose 1000-2000mg/day)	- Extended release; once - Delayed release: twice daily

Referral: the following patients should be referred to a hospital with neurology service

- Patients with poorly controlled seizure despite optimal dose of two recommended antiepileptic drugs
- When there is a doubt in the diagnosis
- When discontinuation is considered

FURTHER READING

1. R. S. Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia, 58(4):531–542, 2017

2. Gerald Liu, Nicole Slater, Allen Perkins: Epilepsy: treatment options. Am Fam Physician. 2017;96(2):87-96.

3. Jeannine M. Conway and Kimberly B. Tallian. Epilepsy. PSAP 2018 BOOK 3 • Neurology /Psychiatry/Epilepsy

11.5 CEREBROVASCULAR DISEASE

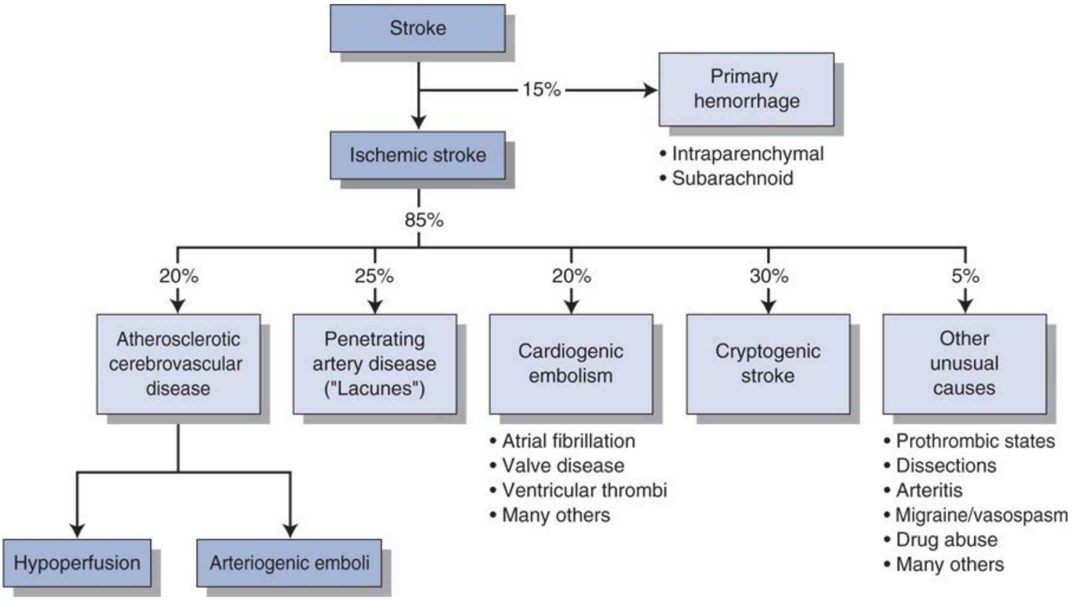
Stroke
15%
Primary hemorrhage
• Intraparenchymal
• Subarachnoid
Ischemic stroke
85%
20%
25%
20%
30%
5%
Atherosclerotic cerebrovascular disease
Penetrating artery disease ("Lacunes")
Cardiogenic embolism
Cryptogenic stroke
Other unusual causes
• Atrial fibrillation
• Valve disease
• Ventricular thrombi
• Many others
• Prothrombic states
• Dissections
• Arteritis
• Migraine/vasospasm
• Drug abuse
• Many others
Hypoperfusion
Arteriogenic emboli

Figure 11: Etiology of stroke

(Redrawn from Verstraete M, Fuster V, Topol EJ, eds. *Cardiovascular Thrombosis: Thrombocardiology and Thromboneurology*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1998:586, Figure 34-2.)

11.5.1. ISCHEMIC STROKE

RISK FACTORS OF ISCHEMIC STROKE

- The most important risk factors are age and HTN. Others include smoking, DM, hyperlipidemia, atrial fibrillation, coronary artery disease

(CAD), family history of stroke, previous stroke/TIA, and carotid bruits.

- In younger patients, risk factors include oral contraceptive use, hypercoagulable states (e.g., protein C and S deficiencies, antiphospholipid antibody syndrome), vasoconstrictive drug use (e.g., cocaine, amphetamines), polycythemia vera, and sickle cell disease.

CLASSES OF ISCHEMIC STROKE

- Transient ischemic attack (TIA)
- Reversible ischemic neurologic deficit is the same as TIA except for the duration of symptoms. It lasts longer than 24 hours, but resolves in less than 2 weeks. This term is not commonly used.
- Evolving stroke is a stroke that is worsening.
- Completed stroke is one in which the maximal deficit has occurred.

TRANSIENT ISCHEMIC ATTACK (TIA)

- TIA is a neurologic deficit that lasts from a few minutes to no more than 24 hours (but usually lasts less than 30 minutes). Stroke may be indistinguishable from a TIA at the time of presentation:
- Duration of symptoms is the distinguishing feature.
- Symptoms are transient with a TIA because reperfusion occurs, either because of collateral circulation or because of the breaking up of an embolus.
- The blockage in blood flow does not last long enough to cause permanent infarction.

EMBOLIC STROKE

- Emboli are a common cause of TIA/CVA
- Possible origins of an embolus include:
    - Heart (most common): due to embolization of mural thrombus in patients with atrial fibrillation.
    - Internal carotid artery.

  - Aorta.
  - Paradoxical: Emboli arise from blood clots in the peripheral veins, pass through septal defects (atrial septal defect, a patent foramen ovale, or a pulmonary AV fistula), and reach the brain.

THROMBOTIC STROKE

- Atherosclerotic plaques may be in the large arteries of the neck (carotid artery disease, which most commonly involves the bifurcation of the common carotid artery), or in medium-sized arteries in the brain (especially the middle cerebral artery [MCA]).

LACUNAR STROKE

- Causes approximately 20% of all strokes; usually affects subcortical structures (basal ganglia, thalamus, internal capsule, brainstem) and not the cerebral cortex.
- Predisposing factor: A history of HTN is present in 80% to 90% of lacunar infarctions. Diabetes is another important risk factor.
- Narrowing of the arterial lumen is due to thickening of vessel wall (not by thrombosis).
- The arteries affected include small branches of the MCA, the arteries that make up the circle of Willis, and the basilar and vertebral arteries.
- When these small vessels occlude, small infarcts result; when they heal, they are called lacunes.

CLINICAL FEATURES OF ISCHEMIC STROKE

- Transient ischemic attack
  - A TIA is usually embolic. However, transient hypotension in the presence of severe carotid stenosis (>75% occlusion) can lead to a TIA.
  - Once a patient has a TIA, there is a high risk of stroke. The risk is increased within days of the TIA; the risk of stroke at 30 days and 5 years is ~10% and 30%, respectively.

  - Evaluation after TIA: brain and neurovascular imaging, ECG and cardiac monitoring, echocardiogram, and labs (CBC, chemistry, lipids, diabetes screening, and others depending on history and risk factors).
- Thrombotic stroke—The onset of symptoms may be rapid or stepwise.
  - Classically the patient awakens from sleep with the neurologic deficits.
- Embolic stroke
  - The onset of symptoms is very rapid (within seconds), and deficits are maximal initially.
  - Clinical features depend on the artery that is occluded.
  - The MCA is most commonly affected, and neurologic deficits seen in MCA involvement include:
    - Contralateral hemiparesis and hemisensory loss.
    - Aphasia (if dominant hemisphere is involved)—for 90% of population this is left cerebral dominance.
    - Apraxia, contralateral body neglect, confusion (if nondominant hemisphere is involved).
- Lacunar stroke—Clinical features are focal and usually contralateral pure motor or pure sensory deficits. Lacunar stroke includes four major syndromes:
  - Pure motor lacunar stroke—if lesion involves the internal capsule.
  - Pure sensory lacunar stroke—if lesion involves the thalamus.
  - Ataxic hemiparesis—incoordination ipsilaterally.
  - Clumsy hand dysarthria.
- Complications of Ischemic stroke
  - Progression of neurologic insult.

  - Cerebral edema occurs within 1 to 2 days and can cause mass effects for up to 10 days. Hyperventilation and mannitol may be needed to lower intracranial pressure (ICP).
  - Hemorrhage into the infarction—rare.
  - Seizures—fewer than 5% of patients.

DIAGNOSIS AND INVESTIGATION

- Initial Assessment
  - History and neurologic exam (including the National Institutes of Health Stroke Scale, NIHSS). The NIHSS score on admission predicts stroke outcomes.
- Brain imaging (CT or MRI)
  - CT scan of the head without contrast is differentiates an ischemic from a hemorrhagic infarction.
  - MRI of the brain is more sensitive than CT; it identifies all infarcts, and does so earlier than CT scan.
- ECG—acute MI or atrial fibrillation may be the cause of embolic strokes.
- Echocardiography: if cardioembolic cause is suspected
- Carotid doppler study
- Labs: RBS, CBC, electrolytes, creatinine, lipid profile, cardiac enzymes and others based on patient factors.

TREATMENT OF ISCHEMIC STROKE

Non pharmacologic

- Supportive treatment (airway protection, oxygen, IV fluids) is initiated. Early recognition of the cause of stroke is unreliable, and early treatment is critical. Therefore, choose therapies that have broad efficacy and safety.
- Assess the patient's ability to protect his or her airway, keep NPO, protect against hypo- or hyperglycemia, avoid fever, and elevate the

head of the bed 30 degrees to prevent aspiration.

- Early referral if better treatment (Thrombolysis) is available, eligible and accessible to the nearest referral Hospital

PHARMACOLOGIC

- Antiplatelet: Aspirin 81-100 mg should be given as early as possible and ideally within 48 hours of stroke onset.
  - Alternative: Clopidogrel 75 mg Po daily
- High dose statin: Atorvastatin 80 mg Po daily
  - Alternative: Rosuvastatin 40 mg Po daily
- Prophylactic Anticoagulants: Unfractionated Heparin 5000 IU SC TID
  - Alternative: Enoxaparin (LMWH) 40 mg SC daily
- BP control—In general, do not give antihypertensive agents in the first 24 hours unless one of the following three conditions is present:
  - The patient's BP is very high (systolic >220, diastolic >120, or mean arterial pressure >130 mm Hg).
  - The patient has a significant medical indication for antihypertensive therapy. Examples include: Acute MI, Aortic dissection, Severe heart failure, Hypertensive encephalopathy.
- Note: Treatment of strokes is prophylactic. Once a stroke has occurred, there is nothing that can be done to salvage the dead brain tissue. The goal is to prevent ischemic events in the future. Specific therapy is recommended.
- The general principles are described below, but please refer specific topics to the guideline
  - Lifestyle and pharmacotherapy for risk factors (HTN, DM, smoking, hyperlipidemia, obesity).
  - Long-term antiplatelet therapy (e.g., aspirin)
  - High intensity statin.

  - Anticoagulation for cardioembolic strokes.
  - Surgery for strokes due to carotid artery disease.

11.5.2. HEMORRHAGIC STROKE

- Two major categories of hemorrhagic stroke:
  - ICH—bleeding into brain parenchyma
  - SAH—bleeding into the CSF; outside brain parenchyma

INTRACEREBRAL HEMORRHAGE (ICH)

BRIEF DESCRIPTION

- Intracerebral Hemorrhage is bleeding in to the brain parenchyma. It is associated with a high mortality rate (50% at 30 days). For those who survive, there is significant morbidity. Hematoma formation and enlargement may lead to local injury and increase in intracerebral pressure.

Causes

- HTN **(**particularly a sudden increase in BP**)** is the most common cause (50% to 60% of cases). HTN causes a rupture of small vessels deep within the brain parenchyma. Chronic HTN causes degeneration of small arteries, leading to microaneurysms, which can rupture easily. It is typically seen in older patients; risk increases with age.
- Ischemic stroke may convert to a hemorrhagic stroke.
- Other causes include amyloid angiopathy (10%), anticoagulant/ antithrombolytic use (10%), brain tumors (5%), and AV malformations (5%).

CLINICAL FEATURES

- Abrupt onset of a focal neurologic deficit that worsens steadily over 30 to 90 minutes.
- Altered level of consciousness, stupor, or coma

- Headache, vomiting
- Signs of increased Intra cranial pressure (ICP)
- Pupillary findings in ICH and corresponding level of involvement
    - ○ Pinpoint pupils—pons
    - ○ Poorly reactive pupils—thalamus
    - ○ Dilated pupils—putamen

DIAGNOSIS AND INVESTIGATIONS

- Clinical history, presentation and risk factors
- CT scan of the head diagnoses 95% of ICH (may miss very small bleeds)
- Coagulation panel and platelets—check these to evaluate for bleeding diathesis.

COMPLICATIONS

- Raised intracranial pressure
- Seizures
- Rebleeding
- Vasospasm
- Hydrocephalus
- Syndrome inappropriate ADH secretion (SIADH)

TREATMENT

NON PHARMACOLOGIC

- Admission to the ICU
- ABC's (airway, breathing, and circulation)—airway management is important due to altered mental status and decreased respiratory drive. Patients often require intubation.
- Early referral if there is an access for a better care

PHARMACOLOGIC

- BP reduction
  - Elevated BP increases ICP and can cause further bleeding. However, hypotension can lower cerebral blood flow, worsening the neurologic deficits. Therefore, BP reduction must be gradual.
  - Treatment is indicated if systolic BP is >180 or the MAP is >130.

1. **Labetalol**: Intravenous boluses
   - Initial dose: 10 to 20 mg IV push over 2 minutes
   - Until target is achieved give double the initial dose in 15 minutes (maximum dose: 80 mg/dose)
   - A total maximum dose: 300 mg OR
2. **Labetalol**: Continuous IV infusion
   - Initial: 0.5 to 2 mg/minute.
   - Titrate the dose to a maximum of 10 mg/minute.
   - A total maximum dose: 300mg

- Initial management of elevated ICP includes elevating the head of the bed to 30 degrees and appropriate sedation and pain control.
  - Mannitol is often used to lower ICP

Mannitol 20% solution

- Initial dose 1 g/kg/dose
- Subsequent doses: 0.25 to 5g/kg/dose every 6 to 8 hours
- Administer over 30 to 60 minutes. It should not be given over a long period (as continuous infusion)
- Inspect for crystals prior to administration. If crystals are present, redissolve by warming solution

- If the patient is on anticoagulation or an antiplatelet agent

  - Stop the medications
  - If on Warfarin and INR is supratherapeutic: give fresh frozen plasma

SUBARACHNOID HEMORRHAGE

BRIEF DESCRIPTION

- Subarachnoid hemorrhage is bleeding in the subarachnoid space. Mortality rate can be as high as 40% to 50% at 30 days.

Causes

- Ruptured saccular (berry) aneurysms are the most common cause—has higher morbidity and mortality than other causes.
- Trauma is also a common cause.
- AV malformation.

CLINICAL FEATURES

- Sudden, severe (often excruciating) headache in the absence of focal neurologic symptoms; classic description is "the worst headache of my life" but may also be more subtle.
- Sudden, transient loss of consciousness—in approximately 50% of patients.
- Vomiting (common).
- Meningeal irritation, nuchal rigidity, and photophobia—can take several hours to develop.
- Death—25% to 50% of patients die with the first rupture. Those who survive will recover consciousness within minutes.
- Retinal hemorrhages—in up to 30% of patients.

Complications

- Rerupture—occurs in up to 30% of patients.
- Vasospasm—occurs in up to 50% of patients (more often with aneurysmal SAH); can cause ischemia/infarction and therefore stroke.

- Hydrocephalus (communicating)—secondary to blood within the subarachnoid space hindering normal CSF flow.
- Seizures may occur (blood acts as an irritant).
- Syndrome of Inappropriate ADH secretion (SIADH)

DIAGNOSIS AND INVESTIGATION

- Non-contrast CT scan—identifies the majority of subarachnoid hemorrhages (SAHs). However, CT scan may be negative in up to 10% of cases.
- Perform lumbar puncture (LP) if the CT scan is unrevealing or negative and clinical suspicion is high. LP isdiagnostic. Make sure that there is no papilledema (perform fundoscopic examination).
    - Blood in the CSF is a hallmark of SAH: as opposed to blood from traumatic LP, the blood appearance of the CSF in SAH does not clear as it drains.
    - Xanthochromia (yellow color of the CSF) is the gold standard for diagnosis of SAH. Xanthochromia results from RBC lysis. Xanthochromia implies that blood has been in CSF for several hours and that it is not due to a traumatic tap.

TREATMENT

NON PHARMACOLOGIC

- Bed rest in a quiet and dark room.
- Early referral if neuro-radio-surgical intervention is available at the next level hospital

Pharmacologic

- Stool softeners to avoid straining (increases ICP and risk of re-rupture).
- Analgesia for headache (acetaminophen 1 gm Po QID).
- IV fluids for hydration.
- Control of HTN—lower the BP gradually because the elevation in BP

may be a compensation for the decrease in cerebral perfusion pressure (secondary to increased ICP or cerebral arterial narrowing).

- Calcium channel blocker (Nimodipine) for vasospasm lowers the incidence of cerebral infarction by one-third.
- Prophylactic anticonvulsant

11.6 VERTIGO

BRIEF DESCRIPTION

- Vertigo refers to a disturbance of the vestibular system characterized by a sensation of spinning or hallucination of movement.
- It is important to identify the common complaint of "dizziness" as vertigo ("room spinning") or lightheadedness (presyncope symptoms from cerebral hypoperfusion).
- The initial goal is to determine whether the cause of the vertigo is peripheral (inner ear) or central (e.g., tumor, CVA).
- Peripheral vertigo is usually benign, but central vertigo can have serious consequences.

CLINICAL FEATURES

- For patient with ongoing symptoms (continuous vertigo), perform a HINTS test to rule out brainstem or cerebellar stroke.
- HINTS is a three-part test and stands for Head Impulse, Nystagmus, and Test for Skew. The presence of all three of the following suggests a peripheral lesion, and is accurate in ruling out a central lesion: abnormal head impulse test, the presence of unidirectional, horizontal, or torsional nystagmus, and absent skew.
- In a patient with vertigo, goal is to differentiate between peripheral (benign) and central (worrisome) vertigo.

CENTRAL VERTIGO

- Gradual onset; other neurologic (brainstem) findings are present in most cases (e.g., weakness, hemiplegia, diplopia, dysphagia, dysarthria, facial numbness).
- Look for cardiovascular risk factors.
- Accompanying nystagmus can be bidirectional or vertical (does not occur in peripheral vertigo).

PERIPHERAL VERTIGO

- Lesions are cochlear or retro cochlear.
- Abrupt onset
- Significant nausea/vomiting
- Head position has strong effect on symptoms.
- Other brainstem deficits are absent, except for tinnitus/hearing loss.

DIAGNOSIS

- Vertigo is a clinical manifestation. Hence, the cause must be established.
- Differentiating central from peripheral vertigo is done clinically. If central vertigo is considered brain imaging (CT or MRI is needed)

TREATMENT FOR PERIPHERAL VERTIGO

- **Benign positional vertigo (BPV)**
  - Vertigo is experienced only in specific positions or during change in position and lasts for a few moments. It has an abrupt onset as soon as the particular position is assumed.
  - Usually presents in patients over 60 years old.
  - Recovery is usually complete (resolves within 6 months).
  - Pharmacologic treatment
    - Meclizine 25-50 mg every 6- 8 hours

      OR

    - Dimenhydranate 50 mg every 6- 8 hours

      OR

    - Dihenhydramine 25-50mg every 6-8 hours

- **Ménière disease**
  - Triad of vertigo, tinnitus, and hearing loss.
  - Attacks may last for hours to days and recur several months or years later.
  - The hearing loss eventually becomes permanent.
  - Treatment
    - Sodium restriction
    - Diuretics
- **Acute labyrinthitis**: due to viral infection of the cochlea and labyrinth; may last for several days.
  - Treatment: treat underlying cause
- **Ototoxic drugs** (aminoglycosides,loop diuretics)
  - Treatment: discontinue or dose reduction offending drug as per the indication
- **Acoustic neuroma** (schwannoma) of the 8th cranial nerve
  - Ataxia, gait unsteadiness, nystagmus, hearing loss, tinnitus.
  - Treatment:
    - Meclizine 25-50 mg every 6- 8 hours

      OR

    - Dimenhydranate 50 mg every 6- 8 hours

      OR

    - Dihenhydramine 25-50mg every 6-8 hours

11.7 GUILLAIN–BARRÉ SYNDROME (GBS)

BRIEF DESCRIPTION

- GBS is an acute inflammatory demyelinating polyneuropathy that primarily affects motor nerves, but has many variants (e.g., Miller Fisher syndrome).
- It is usually preceded by a viral or mycoplasma infection of the upper respiratory or GI tract.
- Other common infections include Campylobacter jejuni, CMV, hepatitis, and HIV.
- It may also occur in Hodgkin disease, lupus, after surgery, or after HIV seroconversion

CLINICAL FEATURES

- Abrupt onset with rapidly **ascending weakness/paralysis** of all four extremities; frequently progresses to involve respiratory, facial, and bulbar muscles.
    - Usually symmetric (but not always).
    - Weakness may be mild or severe.
    - Weakness usually progresses from distal to central muscles.
    - If generalized paralysis is present, it can lead to respiratory arrest.
- Extremities may be painful, but sensory loss is not typical.
- Sphincter control and mentation are typically spared.
- Autonomic features (e.g., arrhythmias, tachycardia, postural hypotension) are dangerous complications.

DIAGNOSIS

- CSF analysis—elevated protein, but normal cell count.

- Electrodiagnostic studies—decreased motor nerve conduction velocity.
- Diagnosis made by a combination of CSF fluid analysis, clinical findings, and nerve conduction velocities.

TREATMENT

NON PHARMACOLOGIC

- Admission to the ICU.
- Carefully monitor pulmonary function.
- Mechanical ventilation may be necessary.
- Early referral if there is no adequate facility to manage

PHARMACOLOGIC

- Administer IV immunoglobulin if the patient has significant weakness. If progression continues, plasmapheresis may reduce severity of disease.
- Referral is needed for this treatment OR consult a specialist
- Note:
    - Do **not** give steroids. They are not helpful in Guillain–Barré syndrome.
    - Prognosis for Guillain–Barré Syndrome
    - Signs of recovery within 1 to 3 weeks after onset favor a good prognosis.
    - If illness continues for a longer period (e.g., beyond 6 weeks), a chronic relapsing course is more likely and prognosis is less favorable.

11.8 BELL'S PALSY

BRIEF DESCRIPTION

- Bell's palsy refers to an acute unilateral infranuclear facial palsy(the entire hemiface affected) with no identifiable cause

- The prognosis is very good; 80% of patients recover fully within weeks to months.

CAUSES

- Cause is often uncertain.
- Possible viral etiology (herpes simplex): immunologic and ischemic factors implicated as well.
- Upper respiratory infection is a common preceding event.

CLINICAL FEATURES

- There is acute onset of unilateral facial weakness/paralysis. Both upper and lower parts of the face are affected.

DIAGNOSIS

- **Clinical, but** Consider EMG testing if paresis fails to resolve within 10 days.

TREATMENT

NON PHARMACOLOGIC THERAPY

- Patient should wear eye patch at night to prevent corneal abrasion (cornea is exposed due to weakness of orbicularis oculi muscle).
- Surgical decompression of CNVII is indicated if the paralysis progresses or if tests indicate deterioration

PHARMACOLOGIC

- If the patient presents within 72 hours of onset
    - Steroid alone for mild to moderate disease
    - Steroid +Acyclovir for severe disease
    - Acyclovir alone should not be given.
    - Dosing

  - – Prednisolone 60-80mg/day for 07 days (no tapering needed)
  - – Acyclovir 400 mg 5 times daily for 7 days

11.9 LOW BACK PAIN

BRIEF DESCRIPTION

- Low back pain is a very common reason for medical consultation and visit.
- Classification:
  - ○ Acute low back pain (LBP) refers to symptoms present for less than 4 weeks,
  - ○ Subacute is 4 to 12 weeks, and
  - ○ Chronic LBP refers to pain lasting more than 12 weeks.
- Risk factors for chronic LBP: smoking, obesity, older age, sedentary work, physically strenuous work, psychologically strenuous work, low educational attainment, worker's compensation insurance, job dissatisfaction,psychological factors (depression, anxiety)

BACK EXAMINATION

- The main goal of the history and physical examination is to rule out any structural or systemic conditions that can be the source of back pain.
- The neurologic examination is very important, and any weakness should be documented.
- The straight leg raise can suggest nerve root compression.
  - ○ The test is positive if radiculopathy is reproduced when the leg is elevated 30 to 60 degrees with the patient supine.
  - ○ If patient is in severe pain and cannot tolerate even a slight elevation of the leg during this test, it is highly suggestive of nerve root compression.

- Look for red flag signs (table below)

Table 11.13: Red flag signs in patients with low back pain

Possible etiology	Symptoms	Signs
Cauda equina syndrome	○ Urinary retention or verflow incontinence ○ New fecal incontinence ○ Progressive motor or sensory loss,	○ Saddle anesthesia ○ Loss of anal sphincter tone ○ Significant motor deficits encompassing multiple nerve roots
Fracture	○ Significant trauma ○ Prolonged corticosteroid use ○ Age older than 70 years, osteoporosis	○ Evidences of trauma
Infection	○ Spinal procedure in the past few months ○ Immunosuppression	○ Fever, wound in the spinal region ○ Localized pain and tenderness
Malignancy	○ History of metastatic cancer ○ Unexplained weight loss	○ Focal tenderness and localized pain in the setting of risk factors

Adapted from ref. Am Fam Physician. 2018; 98(7):421-428

DIAGNOSIS: IMAGING CONSIDERATION

- Most patients with nonspecific low back pain do not need further investigation(imaging)
- Imaging needs to be considered in the following groups of patients
  - ○ Progressive neurologic deficits or disabling symptoms

  - Osteoporosis or prolonged steroid use (suspected osteoporotic fracture)
  - Constitutional symptoms (unexplained fever or weight loss)
  - History of malignancy
  - Recent trauma.
- Patients with the above mentioned exceptions should have an MRI sooner,
- MRI is indicated if patient has failed a course of conservative treatment (physical therapy, NSAIDs) for at least 3 months.

TREATMENT

- General principles
  - Most patients with acute LBP have improvement or resolution within 3 to 6 weeks and are managed with NSAIDs, acetaminophen, activity modification, and gradual return to activities.
  - Narcotic analgesics and muscle relaxants should be used judiciously, if at all.
  - Patients should be advised to continue ordinary activities within the limits permitted by pain.
  - If symptoms do not improve in 4 to 6 weeks, a course of physical therapy for core-strengthening exercises may be helpful.
  - If neurologic deficits present, particularly if these deficits are progressive, a more aggressive approach is indicated. An MRI should be obtained.
  - If nerve root or spinal cord compression is present, evaluation by a specialist is needed.
- The treatment of chronic nonspecific LBP is challenging.

Most patients with chronic LBP with or without radiculopathy are treated conservatively (with physical therapy, NSAIDs, injections).

- Physical therapy is focused on core-strengthening exercises and aerobic conditioning.

- If conservative measures fail and symptoms persist for at least 1 year

REFERRAL

- Patients with red flag signs or progressive neurologic defict should be referred for a neurologist evaluation

FURTHER READING

1. Steven Agabegi, Elizabeth Agabegi. Step-Up to Medicine. 5th edition, 2020.
2. Joshua Scott Will, David C. Bury, and John A. Miller. Mechanical Low Back Pain. Am Fam Physician. 2018; 98(7):421-428

CHAPTER 12:

ONCOLOGY

12.1 BREAST CANCER

BRIEF DESCRIPTION

- Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide.
- In Ethiopia it is the leading cause of female breast cancer accounting for about 22.6% of all female cancers according to GLOBOCAN 2018.
- It is also the leading cause of cancer death among females in Ethiopia.
- The incidence rate is decreasing in North America because of screening and early detection but increasing in other parts of the world.
- Depending on the etiology, breast cancer is classified as sporadic (70% - 80 %), familial (15% - 20 %) and hereditary (5% -10 %).
- Sporadic breast cancer is sub classified as hormonal and non-hormonal.
- Risk factors
    - Hormonal breast cancer is associated with old age, female gender, early age at menarche, late menopause, late age of first pregnancy, nulliparity, dietary fat, obesity and hormone replacement therapy
    - Non-hormonal is associated with radiation exposure during adolescence.

CLINICAL FEATURES

- Asymptomatic: detected during screening
- Symptomatic
    - Painless breast lump

- Thickening or distortion of the breast
- Blood-stained nipple discharge
- Change in color or appearance of areola
- At advanced stages: ulceration, bleeding from ulcer or super infection.
- Orange like breast appearance: diffuse enlargement, reddening and pitting of skin over the breast
- Axillary lymphadenopathy
- Cough or back pain from distant metastases.

STAGING

- TNM staging is the most frequently used staging system.
- AJCC 7th edition TNM staging and group staging of breast cancer is given in the table below.

Table 12.1:TNM staging for breast cancer

TNM status	Definition
T0	No evidence of primary tumor
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	2 cm or less in greatest dimension
T1a	0.5 cm or less in greatest dimension
T1b	0.5 cm but not >1 cm in greatest dimension
T1c	1 cm but not >2 cm in greatest dimension
T2	2 cm but not >5 cm in greatest dimension
T3	5 cm in greatest dimension
T4	Tumor of any size with extension to chest wall and/or skin
T4a	Invasion of chest wall (ribs, serratus anterior, intercostal muscles)

T4b	Edema/'peaud'orange', ulceration, satellite nodules confined to same breast
T4c	Both 4a and 4b
T4d	Inflammatory carcinoma
N0	No lymphadenopathy
N1	Ipsilateral mobile axillary nodes
N2	Ipsilateral axillary nodes fixed to one another or to adjacent structures
N3	Ipsilateral internal mammary node metastases
M1	Involvement of supraclavicular nodes or distant metastases

Group Staging

Tablet 12.2: Group staging using TNM

Stage group	T status	N status	M status
0	Tis	N0	M0
IA	T1	N0	M0
IB	To, T1	N1mi	M0
IIA	T0, T1	N1	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T1, T2	N2	M0
	T3	N1, N2	M0
IIIB	T4	N0, N1, N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

INVESTIGATION AND DIAGNOSIS

- Routine laboratory tests including CBC, RFT, LFT, ALP, and bilirubin direct and total

- Breast imaging
  - Breast ultrasound, mammography or MRI gives important diagnostic clue for breast mass.
  - For those less than 30 year of age ultrasound is the preferred initial imaging
  - For the elderly women one can go directly for mammography.
- Investigating for metastatic disease
  - Chest X-ray
  - Abdominopelvic ultrasound
  - brain CT/MRI and Vertebral CT/MRI : if clinically suspected
- Histopathology
  - It is the only definitive diagnostic modality.
  - Morphologic diagnosis: FNAC or biopsy
  - Immunohistochemistry: To assess hormone receptor status (ER, PR) and Human Epidermal growth factor Receptor – 2 (HER2) statuses which have an implication on management.

TREATMENT

- Depends on the stage of the disease, menopausal status, hormone receptor status and performance status of the patient.
- Surgery, chemotherapy, hormonal treatment, radiotherapy, and targeted therapy are possible available options of treatment.

OBJECTIVES OF TREATMENT

- Cure the disease: Combination of treatment, (non-metastatic breast cancer)
- Increase survival: Metastatic breast cancer
- Improve quality of live: For both non metastatic and metastatic breast cancer

- Addressing aesthetic concerns(disfigurement) and psycho social support: surgical treatment
- Preserve fertility and addressing reproductive health concern

SURGERY

- Most effective when cancer is localized.
- Locally advanced breast cancers need neoadjuvant chemotherapy before surgery.
- All breast cancers need adjuvant chemotherapy after surgery
- All hormone receptor positive breast cancers need adjuvant hormonal therapy after surgery
- Depending on stage and risk stratification most patients need adjuvant radiotherapy
- No role for metastatic breast cancer

CHEMOTHERAPY

- Breast cancer patients who remain disease-free after local and regional treatment alone may eventually relapse and die of overt metastases.
- Chemotherapy reduces or eradicates microscopic systemic metastatic disease in which all macroscopic local tumors have been effectively removed.
- It also decreases the size of mass and makes it operable with free margin.
- Different chemotherapy regimens are available depending on disease factor and patient condition.

HORMONAL THERAPY

- Reduces the annual rate of recurrence and death.
- Also decrease the risk of tumor in the contralateral breast.
- Women with hormone receptor- positive tumor should be offered 5yrs of hormonal therapy.

- Drugs commonly used includes tamoxifen if pre-menopausal or Aromatase inhibitors (Anastrozole/Arimidex, Letrozole, Exemestane) if post-menopausal women.

RADIOTHERAPY: IN DESIGNATED CENTERS

- Indicated after mastectomy in patients with high risks of local recurrence: large tumor size, positive lymph nodes, extensive lymphovascular invasion, or positive surgical margin.
- Also indicated in conservative breast surgery (lumpectomy) so as to decrease local recurrence rate.

SCREENING AND EARLY DETECTION

- Regular self-breast-examination is recommended.
- Screening is recommended with breast ultrasound, mammography and MRI.
- Appropriate workup of any breast lump is important.
- All breast lumps need pathologic confirmation unless the patient put on strict follow up.

PREVENTION

- Life style modification
    - Eliminating alcohol and tobacco consumption
    - Maintaining ideal weight
    - Exercising on a regular basis
- Risk reduction surgeries (bilateral total mastectomy and salpingo-oopharectomy)
    - If positive family history and genetic testing reveals BRACA I Positivity

FURTHER READING

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12.2 CERVICAL CANCER

BRIEF DESCRIPTION

- Cervical cancer is the second most common cancer among women worldwide.
- It is the most common cause of cancer deaths among women in developing countries.
- Ranks as the second most frequent cancer among women in Ethiopia.
- Accounted 9.3% of all female cancer cases and 16.5% of female cancer case deaths in Ethiopia according to GLOCAN 2018.

RISK FACTORS

- Human papillomavirus (HPV) is the main causative agents for cervical cancer.
- Persistent infection of HPV result in cervical intraepithelial neoplasia (CIN).
- HPV 16 and 18 that are most clearly linked to CIN.
- HPV infection is associated with sexual activity, being increased in women starting intercourse at an early age and having multiple partners.
- HPV is more common in women who are or who have been married than

in single women.

- Other recognized etiological factors includes smoking, repeated trauma, miscarriage, multiparity, longer use of oral contraceptives, and co-infection with sexually transmitted diseases.
- It is a recognized HIV related malignancy.

CLINICAL FEATURES

- Asymptomatic
  - Precancerous lesions and early invasive lesions are usually asymptomatic.
- Dyspareunia
- Vaginal bleeding (usually contact bleeding; e.g. after intercourse)
- Vaginal discharge
- Hematuria or rectal bleeding: local spread
- Low back pain
- Anorexia, weight loss, and weight loss
- Features of renal failure: in advanced disease due to bilateral ureteric obstruction,
- Local pain presents when there is extensive pelvic infiltration.
- Pelvic examination
  - Proliferative or ulcerative growth or diffuse infiltration of the cervix
  - Extension on to the vaginal mucosa can be seen
  - Extension in to the parametrium can be noted

STAGING

- The FIGO staging system is commonly used for cervical cancer staging. It is based predominantly on the extent of the primary tumor.

Table 12.3: FIGO staging system

Stage	Definition
IA	Micro-invasive disease (max depth 5 mm, max width 7 mm)
IB	Clinical disease confined to the cervix
IIA	Disease involves upper 1/3 vagina but not parametrium
IIB	Disease involves parametrium but does not extend to pelvic wall
IIIA	Disease involves lower 2/3 vagina
IIIB	Disease involves pelvic wall, presence of hydronephrosis
IV	Involvement of bladder, rectum, or distant organs

INVESTIGATION AND DIAGNOSIS

- Routine laboratory tests
  - CBC: anemia from bleeding or renal involvement.
  - RFT, LFT, ALP, and bilirubin direct and total
- Cervical biopsy and histopathology
  - Definitive diagnosis requires biopsy and histopathology
- Imaging
  - Abdominopelvic CT/MRI: to evaluate cervical mass with its extent; including lymph node involvement
  - CXR and abdominopelvic ultrasound: to assess distant metastasis.
- Cytology (PAP smear), visual inspection with acetic acid (VIA), and human papillomavirus (HPV) tests: are done for screening precancerous lesions.

TREATMENT

OBJECTIVES OF TREATMENT

- Cure the disease: Combination of treatment, non-metastatic cervical cancer
- Increase survival: Metastatic cervical cancer

- Improve quality of live: For both non metastatic and metastatic cervical cancer
- Addressing reproductive health concern and Psychosocial support

PRECANCEROUS LESIONS TREATMENTS

- Cryotherapy
- Large loop excision of the transformation zone (LEEP/LLETZ)
- Cold knife conization (CKC)
- Surgery for CIN III

SURGERY

- Wertheim's hysterectomy for stage IA to II A
- All needs adjuvant radiotherapy after surgery

RADIOTHERAPY AT A DESIGNATED CENTER

- Mainstay of treatment for cervical cancer.
- Cervical cancer is radiosensitive
- As adjuvant for stage IA to IIA
- Definitive radiotherapy for stage IIB to IVA with cure intent
- Receives external beam radiotherapy and intracavitary brachytherapy as a boost
- Hemostatic radiotherapy to arrest bleeding
- Palliative radiotherapy to increase survival, decrease discharge and manage pain in metatstatic condition
- Bleeding, stricture, ulceration, fistula, vaginal shortening/dryness are the possible toxicities

CHEMOTHERAPY

- No established role in the radical treatment. Induction chemotherapy may be used to help in delaying micro metastasis.

- Concurrently given with radical dose radiotherapy
- For recurrent pelvic or systemic metastatic disease

PREVENTION

- Extended natural history makes cervical cancer potential area for successful prevention and early curative intervention.
- Early screening is important
- Patients with cervical bleeding or discharge needs appropriate workup including biopsy.

FURTHER READING

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2. Benoit, Brown, Edwards. Gynecologic oncology handbook, evidence based guideline. Demos Medical Publishing, LLC; 2013.
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12.3 COLORECTAL CANCER

BRIEF DESCRIPTION

- Third most commonly diagnosed cancer case worldwide in both sexes.
- Fourth deadliest disease cancer according to GLOBOCAN 2018.
- It is the leading cause of cancer in males and the fourth cancer incidence in females in Ethiopia.

RISK FACTORS

- About 65% - 80% are sporadic, while 20 – 35% have a hereditary component.
- Presence of adenomatous polyps
- Family history

- Inflammatory bowel disease
- Dietary habits like consumption of red meat, animal and saturated fat, refined carbohydrates and alcohol
- Physical Inactivity, obesity, smoking and race

CLINICAL FEATURES

- Gastrointestinal bleeding
    - Overt lower GI bleeding
        - Bright blood: left sided colon cancer
        - Melena: right sided colon cancer
    - Occult bleeding presenting as iron deficiency anemia (symptoms of anemia)
- Change in bowel habits
- Abdominal pain
- Weight loss
- Loss of appetite
- Fatigue
- On physical examination
    - Palpable mass
    - Bright blood per rectum (usually left-sided colon cancers or rectal cancer) or melena (right-sided colon cancers), or lesser degrees of bleeding (occult positive stool).

STAGING

- TNM staging is commonly used to stage colorectal cancer.

Table 12.4: colorectal cancer staging

TNM staging	Definition
Tis	Carcinoma in situ
T0	No evidence of primary
TX	Primary cannot be assessed
T1	Involving submucosa
T2	Involving muscularis propria
T3	Involving subserosa, non-peritonealized pericolic/perirectal tissues
T4	Other organs/structures/visceral peritoneum
N0	No regional lymphadenopathy
N1	3 or fewer pericolic/perirectal lymph nodes
N2	>3 pericolic/perirectal lymph nodes
N3	Nodes on named vascular trunk/apical node(s)
M0	No distant metastases
M1	Distant metastases

GROUP STAGING

Table 12.5: Group staging for colorectal cancer

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
	T2	N0	M0
IIA	T3	N0	M0
IIB	T4	N0	M0
IIIA	T1-T2	N1	M0
IIIB	T3-T4	N1	M0
IIIC	Any T	N2	M0
IV	Any T	Any N	M1
0	Tis	N0	M0

INVESTIGATION AND DIAGNOSIS

- CBC: microcytic anemia
- Stool for occult blood
- Colonoscopy (rectosigmoidocolonoscopy)
    - Needed in all patients to make a diagnosis: visualizing the lesion, location characterizing and taking specimen for biopsy
- CT colonography (also called virtual colonoscopy)
- Histopathology
    - Definitive diagnosis needs histopathology
- Staging investigation
    - Abodominopelvic CT or MRI
    - Pelvic MRI: for rectal cancer
    - Chest X-ray
    - Abdominopelvic ultrasound
    - Liver enzymes: elevated alkaline phosphatase might indicate liver metastasis
- Carcinoembryonic antigen (CEA)
    - Has low sensitivity for diagnosis; hence, it should not be used for screening
    - It should be done before and after surgery: to evaluate residual disease and recurrence.
    - Routine chemistry: renal function test, liver enzymes

TREATMENT

OBJECTIVES OF TREATMENT

- Cure the disease: for both non metastatic and metastatic colorectal cancer

- Increase survival: for metastatic non resectable disease
- Improve quality of life: for both non metastatic and metastatic colorectal cancer

SURGERY

- The mainstay of curative therapy for localized colorectal cancer
- Curative resection requires the excision of the primary tumor and its lymphatic drainage with an enveloping margin of normal tissue.
- Local excision, low anterior resection (LAR) or abdominoperineal resection (APR) are possible surgical managements for rectal cancer.

CHEMOTHERAPY

- As adjuvant after surgery
- The aim of adjuvant chemotherapy is to eradicate these micro-metastases and thereby prevent future relapse.
- Indication depends on risk stratification of patients.
- Chemotherapy is also the main stay of treatment for advanced colorectal cancer where resection is not possible or in metastatic condition where metastatectomy cannot be done.
- AS neoadjuvant with radiotherapy for rectal cancer.

RADIOTHERAPY IN A DESIGNATED CENTER

- Rectal cancer
    - Radiotherapy is the mainstay treatment for rectal cancer as neoadjuvant or adjuvant concurrent chemoradiotherapy to be followed by surgery
- Colonic cancer

Itis use is limited to the palliative situations e.g. painful bone metastases, skin secondaries, and occasionally for tumors with local infiltration into surrounding organs.

PREVENTION

- Consumption of dietary fiber, vegetables, fruits, antioxidant vitamins, calcium and folate (B vitamin) are found to be protective of colorectal cancer.
- Screening
    - Stool for occult blood
    - colonoscopy

FURTHER READING

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12.4 HEPATOCELLULAR CARCINOMA

BRIEF DESCRIPTION

- Primary liver cancer is the sixth most common cancer and the third most common cause of death from cancer worldwide.
- Ethiopia: primary liver cancer is eleventh top cause of cancer case and death in both males and females.
- Besides primary liver cancer, metastatic liver cancer is the commonest type of liver cancer.

RISK FACTORS

- Hepatitis B and Hepatitis C virus increased incidence of hepatocellular carcinoma.
- Other risk factors
  - Liver cirrhosis of any cause
  - Alcoholic liver disease
  - Autoimmune hepatitis
  - Nonalcoholic fatty liver disease (NAFLD).
  - Cryptogenic cirrhosis
- Potential chemical carcinogens: Aflatoxin B1, anabolic steroids and estrogens

CLINICAL FEATURES

- Non-specific symptoms: poor appetite, weight loss, fatigue,
- Abdominal symptoms
  - Abdominal pain
  - Abdominal swelling or fullness
  - Nausea, vomiting, hematemesis
- Physical findings
  - Hepatomegaly
  - Ascites
  - Jaundice
  - Others signs of chronic liver disease: dilated abdominal veins, palmar erythema, gynecomastia, testicular atrophy and peripheral edema.
- Paraneoplastic features: may be present
  - Hypoglycemia

- Erythrocytosis
- Hypercalcemia
- Carcinoid syndrome: diarrhea, hot flush
- Cutaneous features
- Sexual characteristic changes: testicular atrophy, precocious puberty, gynecomastia,

STAGING

Table 12.6: TNM staging of liver cancer

TNM staging	**Definition**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Solitary tumor without vascular invasion
T2	Solitary tumor with vascular invasion or multiple tumors, none > 5 cm
T3A	Multiple tumors > 5 cm
T3B	Single tumor or multiple tumors of any size involving a major branch of the portal vein or hepatic vein
T4	Tumor(s) with direct invasion of adjacent organs other than the gallbladder or with perforation of visceral peritoneum
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node
N1	Positive regional lymph node
M0	No distant metastases
M1	Distant metastases
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G3	Undifferentiated

GROUP STAGING

Table 12.7: Group staging for liver cancer

Stage	T	N	M
I	T1	N0	M0
II	T2	N0	M0
IIIA	T3a	N0	M0
IIIB	T3b	N0	M0
IIIC	T4	N0	M0
IVA	Any T	N1	M0
IVB	Any T	Any N	M1

INVESTIGATION AND DIAGNOSIS

- Imaging
    - Contrary to most solid tumors the diagnosis depends on imaging; histologic diagnosis is not usually needed.
    - Abdominal ultrasound: any focal lesion >1cm on ultrasound should be subjected for further imaging (multiphase CT scan or MRI)
    - Muti-phase CT scan of the abdomen (Triple phase CT scan of the abdomen) or MRI:
        - Needed for diagnosis
        - Size ≥1 cm, arterial phase hyper-enhancement, a combination of washout, threshold growth, and capsule appearance
- Alpha feto protein (AFP)
    - Has limited role in the diagnosis: it could be normal in patients with HCC or raised in patients with liver disease without HCC.
    - A level >20mcg/l is considered abnormal
    - A very high level >500mcg/l should be considered to be due to HCC
    - Those with HCC and AFP >100mcg/l have poor prognosis

- Percutaneous biopsy
  - should only be performed when diagnostic imaging results are uncertain
  - If there is no background cirrhosis, the diagnosis of HCC cannot be made by imaging alone. Hence, biopsy is needed.
- HBsAg and anti-HCV
- Liver enzymes(LFT), serum albumin, INR

TREATMENT

OBJECTIVES OF TREATMENT

- Cure: in early stages
- Improve survival
- Improve quality of life

OPTIONS OF TREATMENT

- The selection of treatment is determined by the following characteristics
  - Severity of underlying liver disease
  - Patient's performance status
  - The size and vascular supply of the tumor
  - Distribution tumors
- Surgical resection
  - Highly recommended for those with localized disease(T1 or T2) for those without or with compensated cirrhosis.
  - Aim is to cure
- Liver transplantation: treatment of choice for patients with early-stage HCC occurring in the setting decompensated cirrhosis
- Ablation (radiofrequency, microwave, and chemical)

  - For those who do not meet surgical respectability criteria for HCC but still aimed for curative therapy
  - Radiofrequency ablation is superior
- Options for advanced disease who are not candidates for resection , transplantation or ablation: chemoembolization, radio embolization, stereotactic body irradiation and tyrosine kinase inhibitor (sorafenib).

FURTHER READING

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12.5 PROSTATE CANCER

BRIEF DESCRIPTION

- The most common malignant tumour in men over the age of 65 years.
- The second leading cause of cancer deaths in men.
- According to GLOBOCAN 2018 prostate cancer rank third in male cancer by affecting 6.5% of males.

RISK FACTORS

- Age is the most important risk factor.
- High consumption of dietary fats
- Ejaculatory frequency, no of sexual partners, chronic or recurrent infections is also reported as risk factor.
- Prostate cancer is hormone dependent cancer. Androgens are required for the development of prostate cancer.

- Familial risk factor for prostatic cancer is definitely identified.

CLINICAL FEATURE

- Often asymptomatic.
- Detection is usually incidental with PSA value determination and digital rectal examination (DRE).
- Advanced disease gives rise symptoms, but even advanced disease may be asymptomatic.
- The symptoms include bladder outlet obstruction and irritative lower urinary tract symptoms like dribbling, hesitancy, total obstruction, dysuria, frequency and urgency. Pelvic pain, hematuria and hematospermia may present. Bone pain, malaise, 'arthritis', anemia or pancytopenia are symptoms which present with metastasis. Renal failure may develop following obstruction to urinary flow.
- Features on digital rectal examination includes irregular, nodular, stony hard in part or in the whole of the gland, obliteration of the median sulcus, induration is clinical finding on digital rectal examination.

STAGING

- Based upon architectural features of prostate cancer cells, the growth pattern and degree of differentiation, prostate cancer are graded from 1 to 5.
- This is called Gleason grading system.
- It is closely correlates with clinical behavior.

GX	Gleason score cannot be processed
Gleason ≤ 6	Well differentiated (slight anaplasia)
Gleason 7	Moderately differentiated (moderateanaplasia)
Gleason 8-10	Poorly differentiated/undifferentiated (marked anaplasia)

TNM STAGING IS USED TO STAGE PROSTATE CANCER.

Table 12.8: staging of prostate cancer

TNM staging	Definition
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically unapparent tumor, neither palpable nor visible by imaging
T1A	Tumor, incidental finding at TURP (<5% of tissue resected)
T1B	Tumor, incidental finding at TURP (>5% of tissue resected)
T1C	Impalpable tumor identified by needle biopsy because of raised PSA
T2	Tumor confined within prostate
T2A	Tumor involves half of a lobe or less
T2B	Tumor involves more than a half of a lobe but not both lobes
T2C	Tumor involves both lobes
T3	Tumor extends through the prostate capsule
T3A	Unilateral extracapsular extension
T3B	Bilateral extracapsular extension Tumor involves seminal vesicles
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall
N0	No regional lymph node
N1	Positive regional lymph node
M0	No distant metastases
M1	Distant metastases

GROUP STAGING

Tablet 12.9: Group staging for prostate cancer

Stage	T	N	M	PSA	Gleason
I	T1a-c	N0	M0	PSA < 10	Gleason ≤ 6
	T2a	N0	M0	PSA < 10	Gleason ≤ 6
	T1-2a	N0	M0	PSA X	Gleason X
IIA	T1a-c	N0	M0	PSA < 20	Gleason 7
	T1a-c	N0	M0	10 ≤ PSA < 20	Gleason ≤ 6
	T2a	N0	M0	PSA < 20	Gleason ≤ 7
	T2b	N0	M0	PSA < 20	Gleason ≤ 7
	T2b	N0	M0	PSA X	Gleason X
IIB	T2c	N0	M0	Any PSA	Any Gleason
	T1-2	N0	M0	PSA ≥ 20	Any Gleason
	T1-2	N0	M0	Any PSA	Gleason ≥ 8
III	T3a-b	N0	M0	Any PSA	Any Gleason
IV	T4	N0	M0	Any PSA	Any Gleason
	Any T	N1	M0	Any PSA	Any Gleason
	Any T	Any N	M1	Any PSA	Any Gleason
When either PSA or Gleason is not available, grouping should be determined by TNM stage and/or either PSA or Gleason as available.					

INVESTIGATION AND DIAGNOSIS

- PSA level
- All prostate cancer may not have raised level of PSA. When it raised the level is correlates with stage of the disease.
- Transrectal ultrasound guided biopsy as a confirmatory diagnostic tool.
- Routine investigations like CBC is important to detect anemia and thrombocytopenia which can arise from bone marrow infiltration, renal failure or disseminated intravascular coagulation.
- On LFT – raised ALP may suggest hepatic involvement or secondaries in

the bone.

- CXR to detect any lung or rib metastasis
- Pelvic X ray to detect any sclerotic lesions as metastatic tests.
- Abdominopelvic ultrasound helps to see tumor size, renal condition and any visceral metastasis.
- Pelvic and vertebral CT/MRI to detect any metastasis as pelvic bone and vertebra.

TREATMENT

OBJECTIVES OF TREATMENT

- Mostly curative
- Most patients die of comorbid illness than due to prostatic cancer
- Increase overall survival
- Improved quality of live

AVAILABLE TREATMENT OPTIONS

- Surgery (radical prostatectomy – prostatectomy plus orchidectomy), radiotherapy (external beam radiation therapy and brachytherapy), total androgen deprivation therapy, chemotherapy, targeted agents and active surveillance are the available treatment options for prostate cancer.
- Choice of treatment depend on risk stratification.
- Prostate cancer is classified into low, intermediate and high risk depending on TNM staging, Gleason score and PSA level.

ACTIVE SURVEILLANCE

- For early low risk disease, having a PSA<10 ng/mL and a Gleason score <7 have indolent disease, which may never compromise their survival
- Require regular monitoring of the serum PSA, typically every 3 months, with repeat biopsies after 2 years

RADICAL PROSTATECTOMY

- This is indicated for disease that is localized to the gland, i.e. stages T1 and T2.
- After prostatectomy the PSA should be undetectable; any presence of PSA even at very low levels suggests residual prostatic tissue.

RADICAL RADIOTHERAPY

- This is indicated for all patients with disease localized to the pelvis.
- Either external beam radiotherapy or Brachytherapy techniques

HORMONAL THERAPY

- Hormone therapy by androgen deprivation or blockade is effective when first introduced in most patients. It may be used as:
- Primary treatment in frail or medically compromised patients
- Metastatic disease treatment at presentation
- Neoadjuvant or adjuvant treatment
- Relapse after definitive primary treatment
- Anti-androgen drugs include cyproterone acetate, flutamide and bicalutamide. Gonadotrophin-releasing hormone (GnRH) analogue drugs include goserelin and leuprorelin.

CHEMOTHERAPY

- Chemotherapy is treatment will be given for selected patients in metastatic setting with relapse after hormone treatment.

PREVENTION

- Isoflavonoid genistein (which inhibits 5-reductase) found in many legumes and cruciferous vegetables, retinoids (tomatoes, carrot) and statin drugs are reported as protective factors from prostate cancer.
- Screening with PSA and proper digital rectal examination
- Subject specimen for biopsy after any type of prostatectomy

FURTHER READING

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12.7 OVARIAN CANCER

BRIEF DESCRIPTION

- It is the ninth most common cancer and the fourth leading cause of cancer-related death in women worldwide.
- The third commonest cancer among females in Ethiopia accounting 8% from the total.

RISK FACTORS

- The majority of ovarian cancers are sporadic, with about 10% being hereditary.
- Incessant ovulation
- The repeated disruption and repair of the germinal epithelium provide ample opportunity for somatic gene deletions and mutations to occur, which, in turn, can contribute to tumor initiation and progression.
- Excess gonadotropin secretion, promoting high estrogen concentrations, which lead to epithelial proliferation, and, possibly, malignant transformation.
- Advanced age
- Nulliparity
- Infertility
- Diet –saturated fats
- Obesity
- Exposure to talc powder

- Genetics account 10-12 %. A link with the breast cancer-associated genes BRCA1 and BRCA2, as well as with HNPCC, is recognized.

CLINICAL FEATURE

- Can remain asymptomatic for some time and often presents with vague symptoms of abdominal discomfort and pelvic pain.
- In more advanced cases this may be associated with abdominal swelling owing to either tumour or ascites, and urinary and bowel disturbance owing to local pressure.
- An ovarian mass may be palpable per vagina or per rectum and a pleural effusion detectable clinically by dullness to percussion and absent breath sounds.
- A left supraclavicular node may be palpable in advanced cases.

STAGING

- The FIGO staging system for ovarian cancer is in common use:
    - Stage 1 – Confined to the ovary

1a one ovary involved

1b both ovaries involved

- Stage 2 – Spread to the pelvis
- Stage 3 – Spread to the abdominal cavity
- Stage 4 – Blood-borne metastases.

INVESTIGATION AND DIAGNOSIS

- CA 25 level
- Routine investigations like CBC, LFT, RFT and serum electrolyte
- CXR and Abdominopelvic Ultrasound to detect metastases
- CT scan of the abdomen and pelvis will demonstrate the primary tumour and also pelvic and para-aortic lymph node enlargement together with liver metastases if present.

TREATMENT

OBJECTIVES OF TREATMENT

- Improve quality of life
- Improved overall survival, and progression free survival

PRIMARY CYTOREDUCTIVE SURGERY

- Upfront regardless of stage
- Removal of large, poorly vascularized tumor
- Improved chemotherapy delivery
- Increased fraction of G0 resection

CHEMOTHERAPY

- Primary chemotherapy: advanced with newer treatment options for ovarian cancer treatment archives the following
    - Better control of the cancer
    - Significant improvement in overall survival
- Intravenous and intraperitoneal route for chemotherapy delivery is possible
- Intraoperatively the chemotherapy can be administered at time of primary surgery or secondary surgery
- Response classified into three depending on response to chemotherapy:
    - Platinum Sensitivity
    - Platinum Refractory
    - Platinum Resistance
- Second look surgery and/or chemotherapy recommended for relapse depending on the response classification

PREVENTION

- Pregnancy has 13-19% risk reduction
- 50% risk reduction with use of oral contraceptive use for more than 5 years.
- Breast feeding
- Bilateral tubal ligation

FURTHER READING

1. NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer. Including fallopian tube cancer and primary peritoneal cancer. Version 1.2020.
2. Deborah Neesham, Anthony Richards, Melissa McGauran. Advances in epithelial ovarian cancer. AJGP VOL. 49, NO. 10, October 2020.
3. Chyke A. Doubeni; Anna R. B. Doubeni ; And Allison E. Myers. Diagnosis and Management of Ovarian Cancer. Am Fam Physician. 2016;93(11):937-944.

12.8 HEAD AND NECK CANCER

BRIEF DESCRIPTION

- Head and Neck Cancers (HNC) address tumors arising in the lip, oral cavity, pharynx, larynx, and paranasal sinuses; occult primary cancer, salivary gland cancer, and mucosal melanoma (MM).
- Most of them begin in the mucosal surfaces of the upper aerodigestive tract, and these are predominantly squamous cell carcinomas.
- Worldwide, they account for more than 550,000 cases and 380,000 deaths annually.
- Males are affected significantly more than females, with a ratio ranging from 2:1 to 4:1. .
- Nasopharyngeal carcinomas, oral cavity cancers, oropharyngeal cancers, laryngeal and sinonasal cancers are the most common clinically observed head and neck malignancies in Ethiopia.

RISK FACTORS

- The Four Major risk factors
  - Smoking
  - Alcohol consumption
  - Humanpapillomavirus (HPV) infection (especially for oropharyngeal cancers)
  - Epstein-Barr virus (EBV) infection (especially for nasopharyngeal cancers)
- Other Risk Factors
  - Viral infection including Herpes simplex virus and Hepatitis C virus
  - Immunodeficiency
  - Betel nut chewing
  - Occupational exposure
  - Radiation exposure
  - Diet
  - Poor oral Hygiene
  - Genetic factors

CLINICAL FEATURES

- Clinical features depend on the location of tumor.
- Symptoms could be from either the primary site of cancer origin, or from the cervical lymph node metastasis.
- Pain at the site of tumor
- Dysphagia/odynophagia
- Weight loss
- Hoarseness voice

- Swelling/mass lesion
- Otalgia
    - Otalgia as a presenting symptom is significant.
    - Referred otalgia is considered a "red flag" in the evaluation of a patient with a possible head and neck malignancy.
- **Nasopharyngeal carcinoma**
    - Neck mass: regional lymph node metastasis occurs in ~90% of patients.
    - Hearing loss (associated with serous otitis media)
    - Tinnitus
    - Nasal obstruction
    - Adults with a unilateral ear effusion; need nasopharyngeal examination
- **Oral cavity tumors**
    - Mouth pain
    - Non-healing mouth ulcers, bleeding
    - Loosening of teeth or ill-fitting dentures
    - Dysphagia/Odynophagia
    - Weight loss
    - Referred otalgia.
    - Cervical lymphadenopathy
- **Oropharyngeal tumors**
    - Dysphagia/Odynophagia
    - Referred otalgia
    - Obstructive sleep apnea or snoring
    - Oral bleeding

  - Neck mass

STAGING

- Staging of head and neck cancers should be comprehensive and include a complete physical examination, laryngoscopy, and CT/MRI
- TNM system is used for head and neck cancer staging.
- Each anatomical part has its own TNM staging.

INVESTIGATION AND DIAGNOSIS

- Imaging: CT scan or MRI
- FNAC (FNA cytology) or biopsy
  - Lymphadenopathy palpable and accessible: FNA
  - If lymph node is not accessible: ultrasound or CT-guided FNA
  - Open biopsy (surgical): if the findings of the FNAC are inconclusive.
- Endoscopy can be considered to rule out tumor involvement of the cervical esophagus.
- Routine laboratory studies including CBC, LFT, RFT, Bilirubin direct and total

TREATMENT

OBJECTIVES OF TREATMENT

- Mostly the goal is curative
- Improve overall survival and quality of life
- Preserve function
- Addressing cosmetic concerns (disfigurement) and psychosocial support:

PARANASAL SINUS CANCERS

- Management is primarily surgical with adjuvant radiation
- In unresectable and non-operable cases: radiation therapy (RT) should be offered.

- Chemotherapy: limited for the following situations
  - Unresectable but curative-intent therapy in good performance status patients,
  - Postoperatively: positive margins or extracapsular extension of tumor

ORAL CAVITY CANCERS

- Surgery is the preferred initial treatment
- Adjuvant radiotherapy (with or without chemotherapy): for high-risk patients.
- Definitive radiotherapy: for unresectable or non-operable tumors, and tumors in which surgical resection would result in significant functional impairment

OROPHARYNGEAL CANCERS

- Early-stage oropharyngeal cancers can effectively be treated with surgery or radiotherapy.
- The standard of care for locally advanced disease is chemoradiation therapy

LARYNGEAL CANCER

- Early-stage laryngeal cancer: either surgery or radiotherapy
  - The anatomic location and extent of disease will dictate whether surgery is feasible.
- Locally advanced: concurrent chemotherapy and radiation.

SALIVARY GLAND TUMOR

- Surgical resection is the mainstay of management. Adjuvant radiotherapy for high-risk pathologies.
- Inoperable or unresectable: definitive radiotherapy

METASTATIC HEAD AND NECK CANCERS

- Chemotherapy

PREVENTION

- Avoid habits including smoking, tobacco, alcohol and other possible related habits
- Proper workup of symptoms during initial presentation

FURTHER READING

1. NCCN Clinical Practice Guidelines in Oncology, Head and Neck Cancers: Version 1.2020 — February 12, 2020

2. Laura Q.M. Chow and Dan L. Longo. Head and Neck Cancer. N Engl J Med 2020; 382:60-72.

3. Daniel E. Johnson, Barbara Burtness, C. René Leemans et al. Head and neck squamous cell carcinoma. NATURE REVIEWS | Disease Primers (2020) 6:92.

4. Devita, Lawrence, Rosenberg, editors. Cancer principle and practice of oncology. Lippincott Williams & Wilkins; 2011.

CHAPTER 13:

PSYCHIATRIC DISORDERS

13.1 ANXIETY DISORDERS, PTSD AND OCD

THERE ARE DIFFERENT TYPES OF ANXIETY DISORDERS:

- **Specific Phobia** –At least 6 months of irrational and persistent fear and marked avoidance of a specific thing, place or circumstance, to the extent that it interferes with normal functioning.
- **Social Phobia** –At least 6 months of noticeable and persistent fear of being negatively evaluated for at least one social or performance situation.
- **Panic Disorder**–At least one panic attack (acute episode of unprovoked, intense fear/distress accompanied by somatic or cognitive symptoms) resulting in worry about having another panic attack.
- **Generalized Anxiety Disorder (GAD)** –At least 6 months of excessive and uncontrollable daily worry about multiple themes (e.g., school, family safety, world issues, natural calamities, friends, personal performance) that results in physical symptoms and functional impairment.
- OCD and PTSD are not considered as anxiety disorder according to DSM 5
- **Post-Traumatic Stress Disorder (PTSD)** – Following an exposure to significant trauma avoidance or re-experiencing of the trauma for at least one month as illustrated by: intense fear, disturbing dreams, flashbacks, helplessness, physiological agitation upon seeing reminders of the event, or disorganized/agitated behavior.
- **Obsessive-Compulsive Disorder (OCD)** – recurrent, intrusive, inappropriate and unwanted thoughts, or images, causing significant anxiety that interfere with usual functioning.

CLINICAL FEATURES

- See specific anxieties

INVESTIGATIONS

- Clinical

TREATMENT OF GENERALIZED ANXIETY DISORDER

Goal of treatment

- To help the patient to cope with anxiety better
- To minimize physical symptoms of anxiety
- To improve functionality

NON-PHARMACOLOGIC

- Cognitive behavioral therapy (cognitive approach to address cognitive distortions, behavioral approach to address somatic symptoms)
- Supportive psychotherapy- in an acutely anxious patient, reassurance and offering comfort

Pharmacologic

- Pharmacotherapy and/or cognitive behavioral therapy can be used as first-line treatment for generalized anxiety disorder (GAD).

First line

- **Fluoxetine**, 20-40 mg /day. Since fluoxetine can initially cause aggravation of anxiety symptoms for brief period, it is wise to add optimal dose of a benzodiazepine for 1-2 weeks, and then taper and discontinue.

  Or

- **Sertraline** 50-150mg/day. The dose can be escalated within 4-6 weeks. Then, with maximum tolerable dose, we shall wait for additional 4-6 weeks.
- If the treatment is not effective, switch to another antidepressant. If the treatment is effective, maintain on the same dose for 9-12 months.

ALTERNATIVES

If no response to SSRI:

- **Imipramine**, P.O., 25-50mg/day. Increase by 25mg based on response up to 150mg. The patient's tolerance will determine the rate of increase and the maximum dose.
- For the first few weeks, additionally benzodiazepine can be given. **Diazepam**, starting at 2.5 to 5.0mg, P.O, once or twice daily and titrated up to 10mg/day two or three times daily based on response. Taper and discontinue within 2 weeks.

TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER (OCD)

- **Fluoxetine**, P.O. 20-80mg, increase dose based on clinical response and side-effect tolerability increase by 20mg every 4-6 weeks.

  OR

- **Sertraline** P.O. 50-200 mg Increase dose based on clinical response and side-effect tolerability increase by 50mg every 4-6 weeks.

  OR

- **Clomipramine** 100-300mg Increase dose based on clinical response and side-effect tolerability increase by 50mg every 4-6 weeks.

DURATION OF TREATMENT

- 1-2 years after symptom remission

TREATMENT OF POST-TRAUMATIC STRESS DISORDER (PTSD)

First line

- If available a trauma-focused psychotherapy that includes exposure should be attempted prior to serotonergic reuptake inhibitors (SRI).

Alternatives

- **Venlafaxine** 37.5 to 75 mg/day starting dose (75 to 375 daily maintenance dose) if available is effective. OR

- **Fluoxetine**, P.O. 20-80mg, increase dose based on clinical response and side-effect tolerability increase by 20mg every 4-6 weeks.

OR

- **Sertraline** P.O. 50-200 mg Increase dose based on clinical response and side-effect tolerability increase by 50mg every 4-6 weeks.

OR

DURATION OF TREATMENT

- Better be treated for 6 months to a year to prevent relapse and recurrence.

13.2 DEPRESSIVE DISORDERS

MAJOR DEPRESSION

- A major depressive or episode syndrome manifests five or more of the following symptoms, present most of the day, nearly every day, for a minimum of two consecutive weeks.
- At least one symptom is either depressed mood or loss of interest or pleasure.
- The symptoms should cause clinically significant distress impairment in social, occupational, or other important areas of functioning and should not due to the direct pphysiologic effects of substance.
- The nine symptoms of major depression
  - Depressed mood
  - Loss of interest or pleasure in most or all activities
  - Insomnia or hypersomnia
  - Change in appetite or weight
  - Psychomotor retardation or agitation
  - Low energy

  - Poor concentration
  - Thoughts of worthlessness or guilt
  - Recurrent thoughts about death or suicide

DYSTHYMIC DISORDER (PERSISTENT DEPRESSIVE SYMPTOM DISORDER)

- It is marked by chronically depressed mood for at least two years.
- Depression is present for most of the day and for more days than not.
- The depressed mood is accompanied by two or more of the following symptoms:
  - Decreased or increased appetite
  - Insomnia or hypersomnia
  - Low energy
  - Poor self-esteem
  - Poor concentration
  - Hopelessness
- These symptoms are less severe than symptoms of major depression.

INVESTIGATIONS

- Primary depressive disorders are diagnosed by syndromic criteria. So, diagnosis depends on clinical history and mental status examination.
- Assessment should include evaluation for suicide risk, a comprehensive medical history, exploration of comorbid psychiatric disorders including substance use, and family history of mental illness
- When depression secondary to medical disorders is suspected, the following investigation could be helpful:
  - CBC
  - Creatinine and BUN

- Liver function tests,
- TSH, free T3, free T4
- VDRL/RPR and HIV test
- B12 and folate levels

TREATMENT

OBJECTIVES

- Prevent suicide
- Full symptom remission
- Improve functionality

NON PHARMACOLOGIC

- Psychotherapy-Cognitive behavioral therapy (CBT),
- Interpersonal therapy (IPT).
- Family therapy,

Pharmacologic

First line

- **Fluoxetine**, starting dose, 20 mg /day P.O., usual total dose per day 20-40mg/day. OR,
- **Sertraline**, starting dose, 50mg/day P.O. usual dose 50-200mg/day

Alternative

- **Amitriptyline**, starting dose 25-50mg/day P.O. Usual total dose per day 75-150mg/day. Increase by 25mg every 3-5 days up to 150mg orally at night by end of second week. The tolerability will determine the rate of increase and the maximum dose.

  OR

- **Imipramine**, oral, 25-50mg/day. Usual total dose per day 75-150mg/day. Increase by 25mg every 3-5 days up to 150mg orally at night by end of second week. The tolerability will determine the rate of increase and the maximum dose.

PRINCIPLES IN DEPRESSION MANAGEMENT

- Admit patients with suicidal tendencies and severe illness and keep under close observation
- Give maximum tolerable dose for at least 6 weeks before deciding a particular antidepressant is not effective.
- Psychoeducation is required: while the side-effects appear early and disappears, the clinical improvement requires 2-4 weeks
- For a first episode continue antidepressants for 9-12 months.
- When antidepressants are discontinued, they should be tapered over two to four weeks except fluoxetine.
- If night sedation is required, Diazepam 5-10mg or Bromazepam 3-6mg/day, oral, can be used for not more than 2 weeks.
- Stop antidepressants immediately if manic swing occurs.
- Evaluate at a minimum of every one-two weeks for six to eight weeks.

PRECAUTIONS TO BE OBSERVED IN ANTI-DEPRESSANT MEDICATIONS (ADAPTED FROM WHO MENTAL HEALTH GAP INTERVENTIONS GUIDE, 2010)

- To avoid overdoses in people at risk of self-harm/suicide, make sure that they have access to a limited supply of antidepressants only (e.g., dispense for one week at a time).
- Adolescents 12 years and older-avoid TCAS and use fluoxetine.
- Monitor adolescents on fluoxetine frequently (ideally once a week) for emergence of suicidal ideas during the first month of treatment.
- Older people-TCAs should be avoided, if possible. SSRIs are first choice.
- Consider the increased risk of drug-drug interaction interactions in the presence of comorbid conditions and give greater time for response (a minimum of 6 – 12 weeks)

- SSRIs are first choice in people with cardiovascular disease. Do not prescribe TCAs to people at risk of serious cardiac arrhythmias or with recent myocardial infarction.

MONITORING PEOPLE ON ANTIDEPRESSANT MEDICATION (ADAPTED FROM WHO MENTAL HEALTH GAP INTERVENTIONS GUIDE, 2010)

- If symptoms of mania emerge during treatment: immediately stop antidepressants and assess for and manage the mania and bipolar disorder.
- If people on SSRIs show marked/prolonged akathisia (inner restlessness or inability to sit still), review use of the medication. Use diazepam (5-10mg / day) for a brief period (1 week) or change to TCAs
- If poor adherence, identify and try to address reasons for poor adherence (e.g., side- effects, costs, person's beliefs about the disorder and treatment).
- If inadequate response (symptoms worsen or do not improve after 4 – 6 weeks): review diagnosis (including co-morbid diagnoses) and check whether medication has been taken regularly and prescribed at maximum dose.
- Switch from one antidepressant to another with care, that is: stop the first medicine; leave a gap of a few days if clinically possible; start the second medicine. If switching is from fluoxetine to TCA the gap should be 1-2 weeks, for example one week.

TERMINATING ANTIDEPRESSANT MEDICATION (ADAPTED FROM WHO MENTAL HEALTH GAP

INTERVENTION'S GUIDE, 2010)

- **Consider stopping** antidepressant medication when the person (a) has no or minimal depressive symptoms for 9–12 months and has been able to carry out routine activities for that time period.
- **Terminate contact** as follows: in advance, discuss with person the ending of the treatment.

- ○ i. For TCAs and most SSRIs (but faster for fluoxetine): Reduce doses gradually over at least a 4-week period; some people may require longer period.
- ○ ii. Remind the person about the possibility of discontinuation/ withdrawal symptoms on stopping or reducing the dose, and that these symptoms are usually mild and self-limiting but can occasionally be severe, particularly if the medications are stopped abruptly.
- ○ iii. Advise about early symptoms of relapse (e.g., alteration in sleep or appetite for more than 3 days) and when to come for routine follow-up.

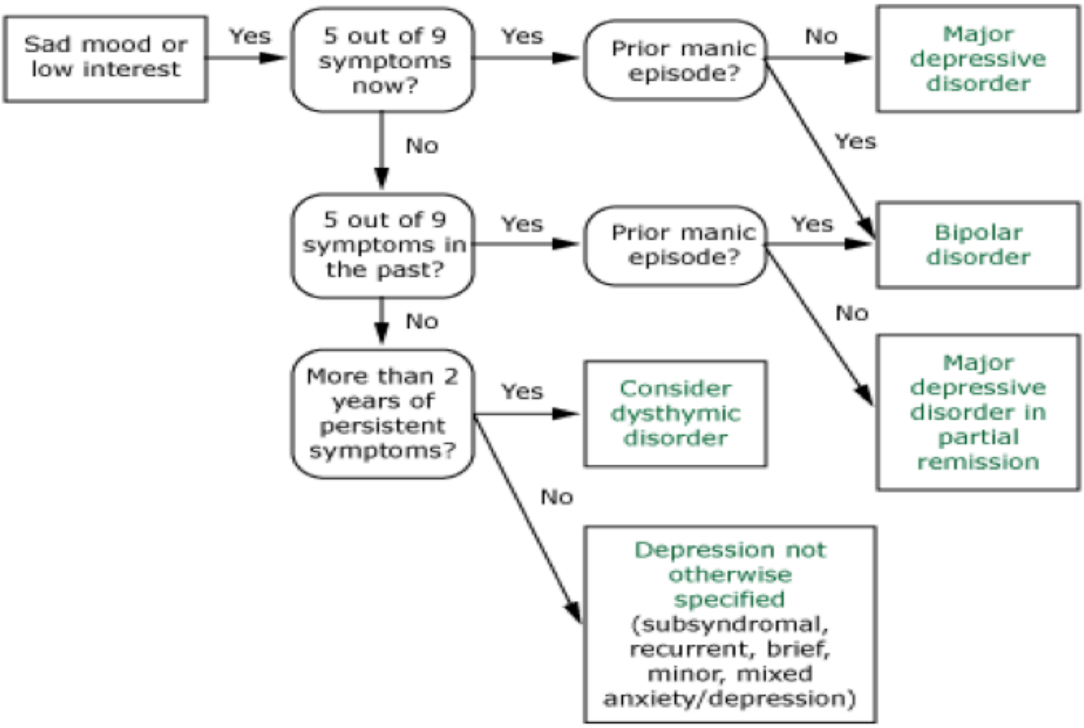

Sad mood or low interest
Yes
5 out of 9 symptoms now?
Yes
Prior manic episode?
No
Major depressive disorder
Yes
No
5 out of 9 symptoms in the past?
Yes
Prior manic episode?
Yes
Bipolar disorder
No
Major depressive disorder in partial remission
No
More than 2 years of persistent symptoms?
Yes
Consider dysthymic disorder
No
Depression not otherwise specified (subsyndromal, recurrent, brief, minor, mixed anxiety/depression)

Figure 13.1. Algorithm for depression

Source: Standard treatment guideline for General Hospitals in Ethiopia, 2014

13.3 BIPOLAR SPECTRUM DISORDERS

BRIEF DESCRIPTION

- Bipolar I disorder: - has episodes of mania, and often depressive episodes.
- Bipolar II disorder: - has one or more major depressive episodes, with at least one hypomanic episode.
- Recognition of bipolar disorder is important; if untreated it is associated with substantial morbidity and mortality, and treatment differs from that of unipolar depression.

CLINICAL FEATURES

- Bipolar disorder is characterized by unpredictable swings in mood from mania (or hypomania) to depression.
- In bipolar II disorder the full criteria for mania are lacking, the recurrent depressions are separated by periods of mild activation and increased energy (hypomania)

DIAGNOSTIC CRITERIA FOR MANIC EPISODE

- Is based on Diagnostic and statistical manual-5 criteria (DSM-5):
- Distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary) with three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
    - Inflated self-esteem or grandiosity
    - Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
    - More talkative than usual or pressure to keep talking
    - Flight of ideas or subjective experience that thoughts are racing
    - Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)

  - Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
  - Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying, sexual indiscretions, or foolish business investments)
- The symptoms do not meet criteria for a mixed episode.
- The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning, usual social activities, or relationships with others; necessitates hospitalization to prevent harm to self or others, or has psychotic features.
- The symptoms are not due to the direct physiological effects of a substance (e.g., a medicine of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

TREATMENT

OBJECTIVES OF TREATMENT

- The objectives of treatment vary based upon the patient's current stage of illness:
  - The acute phase (days to weeks) - Protect patient's safety, preventing suicide and controlling symptoms.
  - The continuation phase (weeks to months) - Prevent relapse of the mood episode.
  - The maintenance phase (months to years) - Prevent recurrence of a new mood episode.

Non pharmacologic

- Psychotherapy
- Family-focused Psychoeducation
- Interpersonal social rhythm therapy (IPSRT)

PHARMACOLOGIC

ACUTE MANIA, HYPOMANIA OR MIXED STATE

First line

- **Sodium valproate**, initial dose.250mg P.O., BID to TID; Dose should be increased by 250-500mg every 1-5 days as tolerated. The goal is a dose of 1500-2500mg/d, max 60mg/kg per day

  OR

- **Carbamazepine**, starting dose of 100-200mg P.O., one or two times per day; Dose should be increased by 200mg /day every 1 to 5 days. The goal is a dose of 800 to 1000mg/day.

  Plus

- **Olanzapine**, starting dose of 5 mg po daily; dose should be increased by 5 mg every third day at maximum. The goal for manic presentation is 10-20 mg per day once or divided twice a day. For maintenance treatment the lowest effective dose should be used. **OR,**
- **Lithium**, P.O., starting dose 300mg BID to TID; Dose should be increased by 300 every 1-5 days based upon response and tolerability. The goal is to reach to a dose of 900-1200mg/day
- Additionally, Diazepam 5-20mg/day in divided doses could be added for agitated patients
- For severely sick patients start a combination of second-generation antipsychotic (e.g., Risperidone, Olanzapine)), Sodium Valproate, and Carbamazepine could be used.

CAUTION ON LITHIUM USE

- Lithium treatment requires close monitoring of serum level, since the medication has a narrow therapeutic range and might cause serious toxicity above the therapeutic window.
- In addition, thyroid and renal function must be checked every 6 – 12 months.

- If laboratory examinations are not available or feasible, lithium should be avoided.
- Erratic compliance or stopping lithium treatment suddenly may increase the risk of relapse. Do not prescribe lithium where the lithium supply may be frequently interrupted.
- Psycho-education should be given about the importance of hydration, early signs of toxicity and interaction with others medication (Antihypertensive, diuretics, NSAIDS) when using lithium

MAINTENANCE THERAPY

- Most patients require maintenance treatment for years, and many for their entire lives with single or combination of the following drugs:
- **Sodium valproate** 750mg/day P.O. in 2-3 dived doses; dose should be increased based on response and tolerability; maximum dose: 60mg/kg/day

AND/OR

- **Olanzapine** 10-20mg/ day P.O in 2 divided doses.

OR

- **Risperidone** 1-6mg/ day P.O in 2 divided doses.
- **Carbamazepine** 400mg/day P.O in 2 divided doses, adjust dose according to response and tolerability by 200 mg/day increments; maximum dose: 1600mg/day

AND/OR

- **Lithium** 900-1200mg/day P.O in 3-4 divided doses or 900-1200mg/day in two divided doses. For extended-release preparations, it can be given once daily.

13.4 SCHIZOPHRENIA

BRIEF DESCRIPTION

- Schizophrenia is a severe psychiatric disorder with chronic or recurrent psychosis and marked functional impairment. It is one of the most disabling and economically catastrophic disorders.
- Psychosis is a break with reality with delusions, hallucinations, disorganized or illogical thinking, and chaotic behavior. Although psychosis is a hallmark of schizophrenia, it is not pathognomonic for the disorder.

CLINICAL FEATURES

- **'Positive' symptoms**
    - Hallucinations
    - Delusions
    - Incoherent speech or illogicality
    - Odd or disorganized behavior
    - Disorders of thought possession
- **'Negative' symptoms**
    - Poverty of speech or of content of speech
    - Apathy
    - Reduced social contact or withdrawal
    - Flattened effect (showing little facial expressive responses) Delusions may be persecutory (undue suspicion) or bizarre

INVESTIGATION

- CBC
- Renal function tests, liver enzymes
- HIV test
- FBS

TREATMENT

OBJECTIVES OF TREATMENT

- Abolish symptoms and restore functioning to the maximum level possible
- Reduce the chances of recurrence
- Avoid or minimize side-effects

NON PHARMACOLOGIC

- Supportive psychotherapy
- Vocational rehabilitation

Pharmacologic

- Antipsychotic medicines are the mainstay of treatment.

EMERGENCY PHASE

First line

- **Haloperidol**, 5-10mg I.M./I.V. every 30-60 minutes till behavioral control is achieved or side effects emerge. Daily dose may go as high as 20mg.
- **Diazepam**: 5-10 mg slow IV is encouraged as adjuvant treatment with IM haloperidol. The dose can be repeated every 30-60 minutes together with haloperidol. This strategy helps to decrease the dose of haloperidol needed to effectively control behavioral disturbance.
- If diazepam is used alone, due to absence of haloperidol or any other reason, higher dose of diazepam may be needed to bring behavioral control. It is wise to start low and go slow till desired effect is achieved.
- Oral haloperidol and/or diazepam can be given if the patient can take oral medications. Dose is similar to parenteral route, but dose repetition can be less frequent, e.g. every 2-4 hourly to allow for full absorption.
- There is risk of severe extrapyramidal side effects with haloperidol IV use

STABILIZATION PHASE

- There is comparable efficacy among antipsychotics, the difference lies in side effect, cost, availability, use in comorbid illness, patient preference

FIRST LINE

- **Chlorpromazine** 300-800 mg/P.O., in divided doses. Increase dose 100mg within 2-3 days based on clinical response and side-effects

  OR

- **Haloperidol**, 1-15mg/day P.O.

SECOND LINE

- **Risperidone:** 1-6 mg orally daily once or divided twice daily.

  OR

- **Olanzapine**: 5-20 mg oral dose once daily or divided twice daily.

MAINTENANCE THERAPY

FIRST LINE

- **Chlorpromazine**, 75-300mg/day P.O

  OR

- **Haloperidol,** 1-15mg/day P.O. QD. in divided doses.

  OR

- **Risperidone**, 1-6mg P.O in divided doses

  OR

- **Olanzapine**, 5-20mg P.O in divided doses
- **Fluphenazine decanoate**, 12.5-50mg IM every 3-4 weeks

INDICATION FOR DEPOT I.M. ANTIPSYCHOTIC

- Refusal to take P.O. medication or non-adherence/partial adherence

DURATION OF TREATMENT

- First episode 1-2 years
- Recurrent 5 years to life

OTHER DISORDERS WITH PSYCHOTIC FEATURES

SCHIZOAFFECTIVE DISORDER

- Schizoaffective disorder has features of both schizophrenia and mood disorders.
- The clinician must accurately diagnose the affective illness, making sure it meets the criteria of either manic or depressive episode but also determining the exact length of each episode.

TREATMENT

- The pharmacotherapy and psychotherapy for schizophrenia apply to patients with schizoaffective disorders.
- Patients with schizoaffective disorder need additional treatment with antidepressants or mood stabilizers for optimal treatment of affective symptoms.
- For the treatment of depressive and manic episodes in schizophreniform disorders, refer the guidelines for the treatment of depressive disorders and bipolar disorders.

SCHIZOPHRENIFORM DISORDERS

- Patients who have all the symptoms of schizophrenia, but for less than six months, are diagnosed with schizophreniform disorder.
- The symptoms of schizophreniform disorder are similar to those of schizophrenia; however, the symptoms last for at least 1 month but less than 6 months.
- Patients with schizophreniform disorder return to their baseline level of functioning after the disorder has resolved.

TREATMENT

- The treatment is like schizophrenia. But the duration should be for 3-6 months.
- But if patients progress to full blown schizophrenia, treatment should be consistent with schizophrenia.

BRIEF PSYCHOTIC DISORDER

- Brief psychotic disorder is a psychotic condition that involves the sudden onset of psychotic symptoms, which lasts 1 day or more but less than a month. Remission is full.

TREATMENT

- Risperidone P.O. 2-6 mg per day
- Haloperidol P.O. 1-15 mg per day
- Treatment duration should be less than a month unless symptoms persist. In which case, revise diagnosis and treat accordingly.

ANTIPSYCHOTIC DRUG SIDE EFFECT MANAGEMENT

EXTRAPYRAMIDAL SYMPTOMS

- Medication induced movement disorders are commonly associated with the use of psychotropic drugs.
- The most common neuroleptic related movement disorders are acute akathisia, parkinsonism, acute dystonia, tardive dyskinesia and neuroleptic malignant syndrome:

Akathisia:

- It is a subjective feeling of restlessness inability to sit still & functionally motor restless (fidgeting, pacing) in sever forms

Akathisia management

- Beta blockers (e.g., **propranolol** up to 160 mg daily, **nadolol** (up to) 80 mg daily, or **metoprolol** 100 mg daily or less)) are effective if given for a few days to a week

- Anticholinergic agents like benztropine can be used as alternative (but not good or may be disappointing for akathisia)
- Reduction in antipsychotic dose is a good intervention but not a realistic goal in an acutely psychotic patient
- Switch to an antipsychotic with a lower risk of akathisia (e.g.Aripiprazole or Quetiapine) or an antipsychotic previously used in the patient without adverse effect.

PARKINSONIAN SYNDROME (SECONDARY PARKINSONISM OR PSEUDO-PARKINSONISM):

- Tremor at rest, akinesia, bradykinesia, stoop gait
- The onset of symptoms is typically 1 to 2 weeks after initiation of antipsychotic therapy or a dose increase
- Drug type (first generation antipsychotics), dose (high), increasing age (elderly) and possibly female gender are risk factors

Parkinsonian management

- Anticholinergics has well established use: **benztropine's** 1-2 mg BID, **trihexyphenidyl** 2-5 mg TID, **diphenhydramine** 25-50 mg TID, **biperiden** 2mg TID for > 2 weeks
- **Amantadine** 100 mg orally two to three times daily for the immediate release form can be used if anticholinergics are not tolerated
- Anti-Parkinson's drugs are not helpful, if used taper and discontinue 6 weeks to 3 months after symptom resolution. Prophylactic antiparkinsonians may be tried if there is a known history of sensitivity to EPS particularly with first generation antipsychotics.
- If symptoms reappear, switching to SGA. Quetiapine, aripiprazole, or clozapine are reasonable alternatives in EPS with other SGAs.

Dystonia

- It is an involuntary contraction or twitches of major muscles. Characterized by torticollis, retrocollis, oculogyric crisis, and opisthotonos. It has a rapid onset, may even occur after first dose and occur/relief within 1-3 days.

DYSTONIA MANAGEMENT

- Sever dystonia: IM or IV anticholinergics (**Benztropine** 1 to 2 mg or **Diphenhydramine** 50 mg) are the treatments of choice. Drugs should be withdrawn after a few weeks.
- Alternatively, benzodiazepines; **Diazepam** 5 to 10 mg by slow IV push or lorazepam 1 to 2 mg IM can be given.
- Mild dystonia: **Trihexyphenidyl** 2-5mg PO TID, **Benztropine** 1 to 2 mg orally once or twice daily.
- After acute treatment of dystonia, preferably change the antipsychotic with a lower EPS liability.
- Prophylactic anticholinergic (**Trihexyphenidyl** 2-5mg PO) is reasonable when using high-potency FGAs (e.g., haloperidol or fluphenazine) in young men, and in patients with a history of dystonia and those with parenteral medications (otherwise not routinely recommended with all FGAs).

TARDIVE DYSKINESIA (TD):

- Involuntary movements of the lips, tongue, face, jaw, extremities, or trunk. TD occurs after chronic use of antipsychotic medications and rarely occurs prior to three to six months of antipsychotic use and usually after years of treatment. No standardized diagnostic criteria for tardive dyskinesia are available.

TD RISK FACTORS INCLUDE:

- First generation antipsychotics (particularly high potency once) has high risk than SGAs (risperidone > olanzapine > iloperidone or low dose quetiapine >> clozapine (no report)),
- Increased dose and duration of treatment
- Increasing age
- Occurrence of acute EPS
- Poor antipsychotic drug response

- Diagnosis of organic mental disorder, diabetes mellitus, mood disorders,
- Overall morbidity and mortality are greater in tardive dyskinesia patients.

TD MANAGEMENT

- Early signs of TD can be reversible but at late stages it become irreversible, even with drug discontinuation. Abnormal involuntary movements can be detected early through physical assessment and the use of rating scales.
- When the antipsychotic dose is decreased or tapered and discontinued, worsening of abnormal movements can occur, followed by possible slow improvement after months or years if the patient remains on lower doses or discontinues treatment.
- **Prevention is key, as treatment is difficult.**
  - Avoid continuous Metoclopramide use for longer than 12 weeks
  - Regular neurologic examinations should be performed at baseline and at least quarterly or biyearly to assess for early signs of TD. The assessment should be more frequent at early stage of the treatment, for those with risk factors.
  - At first signs of TD, assesses the need for discontinuing the antipsychotic immediately
- If continuing treatment is indicated, switch to second generation antipsychotic, Clozapine especially in patients with moderate to severe dyskinesias
  - **Clozapine**
    - Initial dose 25 mg daily, 12.5 to 25 mg increments every one to two days, according to the clinical response and side effect tolerance
    - Maintenance dose: 300 to 600 mg daily.
    - Clozapine requires frequent blood monitoring (weekly WBC monitoring for the first 6 months, biweekly for the next 6 months and then quarterly/year for the remaining duration of treatment) for agranulocytosis

Alternative

- **Quetiapine** in low doses

OTHER TD TREATMENTS

- Benzodiazepine: for mild TD and associated anxiety (use clonazepam 0.5 mg daily, titrate by 0.5 mg increments every five days according to response and tolerance, up to a maximum of 3 to 4 mg/day, if there is no prior benzodiazepine dependence)
- Botulinum toxin injections (variable dosing): localized severe tardive dystonia (e.g., cervical dystonia, blepharospasm)
- Vesicular monoamine transporter 2 (VMAT2) inhibitors: Valbenazine (40 mg daily not for more than six weeks, safety not studied and avoid in long QT syndrome) can be used for disturbing and intrusive TD or tardive dystonia not responsive.
- Anticholinergic: Should be avoided as they exacerbate tardive dyskinesia except in severe debilitating tardive dystonia (trihexyphenidyl, 1 mg BID and titrated to a total dose of 4 to 6 mg daily as tolerated if no narrow-angle glaucoma, confusion and dementia).
- Amantadine (300mg/day) may help as adjunct with antipsychotics.

METABOLIC SIDE EFFECTS

- Weight gain, hyperlipidemia, hyperglycemia, and hypertension, collectively called metabolic syndrome, are risk factor for cardiovascular disease.
- Commonly seen with Olanzapine, risperidone, and clozapine and less commonly with aripiprazole, ziprasidone and haloperidol.
- When starting new medication baseline body mass index, serum lipids, and either fasting blood glucose or hemoglobin A1c has to be done and then more frequent and regular assessment is required.

MANAGEMENT OF ANTIPSYCHOTIC-INDUCED METABOLIC SYNDROME

- Changing the antipsychotic regimen

- Lifestyle interventions (physical activity and diet modification)
- Medication (metformin, topiramate, and adjunctive aripiprazole) and/or psychosocial interventions for individual metabolic risk factors.
- Managing underling metabolic syndromes and risk factors

NEUROLEPTIC MALIGNANT SYNDROME (NMS)

- It is a life-threatening complication that can occur anytime during the course of antipsychotic treatment.
- The motor and behavioral symptoms include muscular rigidity, and dystonia, akinesia, mutism and agitation.
- The autonomic symptoms include hyperthermia, diaphoresis, increased pulse and blood pressure.
- Laboratory findings include increased WBC, increased liver enzymes, creatine phosphokinase, plasma myoglobin and sometimes myoglobinuria.

MANAGEMENT OF NMS

- Stop antipsychotic immediately and begin supportive therapy (these are sufficient in most cases and the role of adjunctive therapy is unclear).
- Medical support with I.V fluids, antipyretics and oxygenation.
- Dantrolene 1mg/kg for 8 days, then continue as P.O. for 7 days, OR
- Bromocriptine 2.5 mg P.O. bid or every eight-hourly max. 45 mg per day
- If needed only SGAs should be used for rechallenge following an episode of NMS, with the lowest dose possible and slower titration and after an extended period (> 2 weeks) of drug free observation of change.

13.5 SUICIDE/SELF-HARM

BRIEF DESCRIPTION

- Suicide is the act of deliberately killing oneself.
- It is a psychiatric emergency which requires urgent evaluation and

management.

- Self-harm is a broader term referring to intentional self-inflicted poisoning or injury, which may or may not have a fatal intent or outcome.
- Any person over 10 years of age experiencing any of the following conditions should be asked about thoughts or plans of self-harm in the last month and about acts of self-harm in the last year:
  - Depression, bipolar disorder, psychosis, alcohol and medicine use disorders
  - Chronic pain
  - Acute emotional distress

EVALUATION AND TREATMENT

- Observe evidence of self-injury and emergency conditions
  - Look for evidences of poisoning or intoxication, bleeding from self-inflicted wound, loss of consciousness, extreme lethargy, if present provide emergency treatment
- Assess for an imminent risk of self-harm/suicide-the presence of one or more of the followings indicate the risk
  - Current thoughts or plan to commit suicide or self-harm
  - History of thoughts or plan of self-harm in the past month or act of self-harm in the past year
  - Severe emotional distress, hopelessness, extreme agitation, violence, uncommunicative behavior, social isolation
  - If there is a risk of imminent self-harm/suicide, take the following measures:
    - Remove means of self-harm.
    - Create secure and supportive environment; if possible, offer separate, quiet room while waiting.
    - Do not leave the person alone.

  - Supervise and assign a named staff member or a family member to ensure safety.
  - Attend to mental state and emotional distress.
  - Offer and activate psychosocial support
  - Maintain regular contact and follow

- Assess for the presence of mental illness, chronic medical illness, neurologic illness, chronic pain or medicine use disorders
  - Depression, bipolar disorder, alcohol or medicine use disorders, psychosis, behavioral disorders, epilepsy, chronic medical illness.
  - If any of these predisposing disorders are present, manage them accordingly.
- Assess for the presence of severe emotional distress that warrant clinical management
  - Difficulty carrying out usual work, school, domestic or social activities
  - Marked distress or repeated help-seeking
  - Repeated self-medication for emotional distress or unexplained somatic symptoms
  - In case of bereavement: support culturally appropriate mourning/ adjustment and reactivate social networks.
  - In case of acute distress after recent traumatic events: offer basic psychological support i.e., listen without pressing the person to talk; assess needs and concerns; ensure basic physical needs are met; provide or mobilize social support and protect from further harm.
  - AVOID psychological debriefing (i.e., DO NOT push the person to recount perceptions, thoughts, and emotional reactions experienced during a recent, stressful event)

Asking about self-harm/suicide DOES NOT provoke acts of self-harm/suicide. It often reduces anxiety associated with thoughts or acts of self- harm and helps the person feel understood. However, try to establish a relationship with the person before asking questions about self-harm/suicide. Ask the person to explain their reasons for harming themselves

13.6 DELIRIUM

BRIEF DESCRIPTION

- Delirium is characterized by an acute decline in both the level of consciousness and cognition with particular impairment in attention.
- Abnormalities of mood, perception, and behavior are common psychiatric symptoms.

INVESTIGATION

- Laboratory work up is important
  - Blood chemistries (including electrolytes, renal and hepatic indexes and glucose)
  - CBC with white cell differential
  - Thyroid function tests
  - HIV test, serologic test for syphilis
  - Urinalysis
  - Electroencephalogram
  - Chest X-ray
  - Additional tests as indicated.

TREATMENT

Goal

- The primary goal is to treat the underlying cause.
- The other important goal is to provide physical, sensory and environmental support.

PHARMACOTHERAPY

- The two targets of pharmacologic treatment in delirium are psychosis and insomnia.

- For psychosis:
    - **Haloperidol** 2-6mg I.M./I.V. to be repeated after an hour followed by oral Haloperidol 5-20mg in two divided doses until symptoms resolve.
- For insomnia:
    - **Lorazepam** 1-2mg at bed time.
    - Benzodiazepine with intermediate and long half-lives should be avoided.

13.7 SUBSTANCE RELATED DISORDERS

BRIEF DESCRIPTION

- Drugs that do have abuse potential:
    - CNS depressants: alcohol, γ-hydroxybutyrate, benzodiazepines and other sedative-hypnotics, and opiates
    - CNS stimulants: cocaine, and methamphetamine
    - other drugs of abuse include: nicotine, methamphetamine analogs, marijuana, phencyclidine (PCP), ketamine, lysergic acid diethylamide (LSD), and inhalants.
- The substance-related disorders include disorders of intoxication, dependence, and withdrawal
- Substance dependence or addiction is a chronic illness that can be successfully controlled with treatment, but cannot be cured, and is associated with a high relapse rate.
- **Addiction**: A primary chronic neurobiological disease, with genetic, psychosocial, & environmental factors influencing its development and manifestations.
    - It is characterized by behaviors that include one or more of the following 5Cs: chronicity, impaired control over drug use, compulsive use, continued use despite harm, and craving.

- **Intoxication:** Development of a substance-specific syndrome after recent ingestion and presence in the body of a substance
    - it is associated with maladaptive behavior during the waking state caused by the effect of the substance on the CNS.
- **Physical dependence:** A state of adaptation that is manifested by a drug class–specific withdrawal syndrome that can be
    - produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.
- **Substance abuse:** A maladaptive pattern of substance use characterized by repeated adverse consequences related to the repeated use of the substance.
- **Substance dependence:** The characteristic feature is a continued maladaptive pattern of substance use in spite of repeated adverse consequences related to the repeated use.
- **Tolerance:** A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.
- **Withdrawal:** The development of a substance-specific syndrome after cessation of or reduction in intake of a substance that was used regularly

TREATMENT OF SUBSTANCE RELATED DISORDERS

Goal of treatment

- Achieving and maintaining abstinence from substance use.
- Harm reduction (reducing use and adverse consequences).
- Addressing associated problems (individual behaviors, family functioning, peer and interpersonal relations, and academic or vocational practices).

Treatment of intoxication

- When possible, drug therapy should be avoided, but may be indicated if patients are agitated, combative, or psychotic.

- When toxicology screens are desired, blood or urine should be collected immediately when the patient presents for treatment.

Table 13.1. Summary of substance use intoxication

Drug class	**Pharmacologic therapy**	**Non-pharmacologic therapy**
Benzodiazepines	Flumazenil 0.2 mg/min IV initially, repeat up to 3 mg maximum	Supportive vital functions
Alcohol, barbiturates and non-benzodiazepine sedative-hypnotics	None	Supportive vital functions
Opiates	Naloxone 0.4 to 2 mg IV every 3 minutes	Supportive vital functions
Cocaine and other CNS stimulants	Lorazepam 2 to 4 mg IM every 30 minutes to 6 hours as needed for agitation Haloperidol 2 to 5 mg (or other antipsychotics) every 30 minutes to 6 hours as needed for psychotic behavior	Monitor cardiac function
Hallucinogens, Marijuana, and inhalants	See above	Reassurance; talk-down therapy; Supportive vital functions
Phencyclidine	See above	Minimize sensory input

TREATMENT OF WITHDRAWAL

- Medically supervised withdrawal should be in place using agonists or other medications that provide symptomatic relief.
- **Treatment of alcohol withdrawal**

  - Multivitamin 1 tab/day for malnutrition
  - Thiamine 50-100mg/day for 3days should be administered for all patients
  - Crystalloids (D5-0.45NS with 20 mEq of KCL per litter) for dehydration
  - Labetalol 20mg IV every two hour as needed for hypertensive urgency,
  - Clonidine 0.05-0.3mg/day for autonomic rebound
  - Electrolyte replacement if low (added to IV solutions)
  - Benzodiazepines (lorazepam 1–2 mg PO/IV/IM is preferred for general practice use due to low liver effect than diazepam) for agitation and seizure
  - Antipsychotics could be used for refractory cases to benzodiazepines
- **Treatment of benzodiazepines withdrawal**
  - The onset of withdrawal from long-acting BZs may be up to 7 days after discontinuation of the drug.
  - Benzodiazepines (Lorazepam0.5-2mg) three to four times a day for 5 days, taper for 5 to 7 days, plus 5 days tapering for long acting BDZ withdrawal
- **Treatment of barbiturates withdrawal**
  - Phenobarbital tolerance test is assessed
  - Initial detoxification at upper limit of tolerance test is done and then decrease dosage by 100 mg every 2 to 3 days
- **Treatment of opiate withdrawal**
  - **Methadone** (20-40 mg/day) orally; tapper by 5-10mg daily for 30-180 days
  - **Buprenorphine** 4 to 32 mg orally daily, titrated to a target 16 mg/day (range, 4 to 24 mg/day). Suboxone can used for maintenance treatment of opiate addiction

  - **Clonidine** 2 mcg/kg three times a day for 7 days, taper over additional 3 days can attenuate the noradrenergic hyperactivity of opiate withdrawal
- **Treatment of mixed substance withdrawal (drugs are cross-tolerant)**
  - Detoxify according to treatment for long-acting drug used
- **Treatment of mixed substance withdrawal (drugs are not cross-tolerant)**
  - Detoxify from one drug while maintaining second drug then detoxify from second drug
- **Treatment of CNS stimulants withdrawal**
  - Supportive treatment only; Pharmacotherapy often not used;
  - **Bromocriptine** 2.5 mg three times a day or higher may be used for sever craving associated with cocaine withdrawal

TREATMENT OF SUBSTANCE DEPENDENCE

- The treatment of drug dependence or addiction is primarily behavioral.
- The goal of treatment is complete abstinence, and treatment is a lifelong process.
- Most drug-dependence treatment programs embrace a treatment approach based on Alcoholics Anonymous.
- **Treatment of alcohol dependence:**
  - **Disulfiram** 250 mg/day, delay the administration at least for 24 hours from the last drink. Have baseline liver function test, repeat at 2 weeks, 3 months, and 6 months, then twice yearly
  - **Naltrexone** 50 to 100 mg/day, monitor LFTs monthly for the first 3 months, then every 3 months.
- **Nicotine dependence treatment:**
  - Nicotine replacement therapy are preferred first line options:

- **Nicotine gum** 2-mg gum if smoking < 25 cigarettes a day, 4 mg if >25 cigarettes a day
- **Nicotine inhaler** or
- **Nicotine nasal spray** 0.5mg delivery to each nostril, 1 mg total for 3 to 6 months
- **Nicotine patch** 16 and 24-hour patches every morning on hairless area for less than 8 months

AND/OR

- **Bupropion** sustained release (150 mg once daily for 3 days, then twice daily for 7 to 12 weeks or longer, then maintaining on 150 mg BID for up to 6 months),
- **Clonidine** 0.1 mg orally BID or 0.1 mg/day transdermally for 3 to 10 weeks

OR

- **Nortriptyline** 25 mg/day, increasing to 75 to 100 mg/day gradually for 12 weeks may be considered if first-line therapy fails (initiate 10 to 30 days before quitting smoking)
- All patients attempting tobacco cessation should be offered practical counseling (problem-solving/skills training), social support, stress management and relapse prevention methods.

CHAPTER 14:

RESPIRATORY DISORDERS

14.1 COUGH

BRIEF DESCRIPTION

- Cough can be divided into acute (less than 3 weeks duration), sub-acute (3 to 8 weeks) and chronic (more than 8 weeks duration).
- If the cause is benign, cough usually resolves in a few weeks.
- If a cough lasts for longer than 1 month, further investigation is warranted.
- In immune-compromised patients, acute cough might need investigation.

CAUSES OF COUGH

- Conditions that are usually associated with other symptoms and signs
  - Upper respiratory infections (URIs): the most common cause of acute cough
  - Pulmonary disease: pneumonia, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, lung cancer, asthma, lung abscess, tuberculosis, CHF with pulmonary edema are some of the causes
- Isolated cough in patients with normal chest radiograph
  - Smoking
  - Postnasal drip: caused by URIs (viral infections), rhinitis (allergic or nonallergic), chronic sinusitis, or airborne irritants
  - Gastroesophageal reflux disease (GERD): especially if nocturnal cough; when lying flat, reflux worsens due to position and decreased lower esophageal sphincter [LES] tone)
  - Asthma: cough may be the only symptom in 5% of cases

  - ACE inhibitors: may cause a dry cough by inhibiting bradykinin breakdown, leading to increased bradykinin production

DIAGNOSIS AND INVESTIGATION

- Usually, no tests are indicated in a patient with acute cough.
- CXR is indicated only if a pulmonary cause is suspected, if the patient has hemoptysis, or if the patient has a chronic cough. It also may be appropriate in a long-term smoker in whom COPD or lung cancer is a possibility.
- CBC if infection is suspected.
- Pulmonary function testing if asthma is suspected or if cause is unclear in a patient with chronic cough.
- Bronchoscopy (if there is no diagnosis after above workup) to look for tumor, foreign body, or tracheal web.
- CT scan is also indicated.
- Those patients who need CT Scan and Bronchoscopy should be referred to the next level health facility

GENERAL PRINCIPLES FOR TREATMENT OF COUGH

- Treat the underlying cause, if known
- Smoking cessation, if smoking is the cause
- Allergic rhinitis, consider a non-sedating long-acting oral antihistamine
- Nonspecific antitussive treatment is indicated in:
  - If cause is unknown (and thus specific therapy cannot be given).
  - If specific therapy is not effective.
  - If cough serves no useful purpose, such as clearing excessive sputum production or secretions.
- Agents used to improve the effectiveness of antitussive medications include expectorants such as guaifenesin and water.

14.2 OBSTRUCTIVE LUNG DISEASES

BRONCHIAL ASTHMA

Definition

- Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.
- It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable airflow limitation.

CLINICAL MANIFESTATION AND DIAGNOSIS

- The diagnosis of Asthma is made clinically using history and physical examination after excluding alternative diagnosis.
- Characteristic pattern of symptoms with wheezing, shortness of breath, cough, chest tightness varying over time and in intensity.
- Symptoms usually get worse during night or early morning and/or with known triggers (Eg, infection, allergy exposure, weather change, exercise, medications, occupational risk and emotional disturbances).
- Peak Expiratory Flow (PEF) can aid the diagnosis.
- Most asthmatics has family history of asthma and has history of wheezing starting from early child hood.

Table 14.1: Symptom based diagnosis of Asthma

Increased probability that symptoms are due to asthma	*Decreased* probability that symptoms are due to asthma
• More than one type of symptom (wheeze, shortness of breath, cough, chest tightness) • Symptoms often worse at night or in the early morning • Symptoms vary over time and in intensity • Symptoms are triggered by viral infections, exercise, allergen exposure, changes in weather, laughter, irritants such as car exhaust fumes, smoke, or strong smells	• Isolated cough with no other respiratory symptoms • Chronic production of sputum • Shortness of breath associated with dizziness, light-headedness or peripheral tingling • Chest pain • Exercise-induced dyspnoea with noisy inspiration (stridor)

- Physical Examination helps in excluding alternative diagnosis. Normal finding doesn't exclude the possibility of asthma.
- Examine the nose, throat and upper airways for (nasal polyp, nasal congestion and/or blockage. Look also for features of Atopy or eczema on the skin.
- The most frequent finding is wheezing on auscultation, especially on forced expiration.
- Silent Chest on chest auscultation might signify severe asthma.
- Wheezing is also found in other conditions, for example: Respiratory infections (Viral), COPD, Upper airway dysfunction, Endobronchial obstruction
- The diagnosis of asthma in general hospital should be based on:

  - A history of characteristic symptom patterns mentioned above with evidence of variable airflow limitation, from PEF, bronchodilator reversibility testing or response to treatment.
    - A 20% or more change in PEF values from morning to afternoon or from day to day or before and after bronchodilator therapy suggests a diagnosis of asthma or inadequately controlled asthma.
    - PEF values less than 200 L/min indicate severe airflow obstruction.
  - A trial of glucocorticoids (e.g. 30 mg daily for 2 weeks) may be useful in establishing the diagnosis, by demonstrating an improvement in either PEF or symptoms.

TREATMENT

GOALS OF ASTHMA MANAGEMENT

- The long-term goals of asthma management are:
  - Symptom control: to achieve good control of symptoms and maintain normal activity levels
  - Risk reduction: to minimize the risk of asthma-related death, exacerbations, persistent airflow limitation and medication side-effects
- Achieving these goals requires a partnership between patient and their health care providers
  - Ask the patient about their own goals regarding their asthma. Shared decision-making is associated with improved outcome.
  - Good communication strategies are essential.
  - Consider the health care system, medication availability, cultural and personal preferences and health literacy.

TREATMENT TO CONTROL SYMPTOMS AND MINIMIZE RISK

- Establish a patient-clinician partnership
- Train every patient in essential skills and guided asthma self-management including:

  - Asthma information
  - Inhaler skills
  - Adherence
  - Guided self-management education
  - Written asthma action plan
  - Self-monitoring
  - Regular medical review.
- Follow the continuous control-based asthma management cycle:
  - Assess symptom control and risk factors
  - Adjust treatment (pharmacological and non-pharmacological)
  - Review the response: symptoms, exacerbations, side effects
- Approaches of Asthma Management
  - Medications: Every patient with asthma should have a reliever medication
  - Most adults and adolescents with asthma should have a controller medication to reduce the risk of serious exacerbations, even in patients with infrequent symptoms
  - Treating modifiable risk factors and comorbidities
  - Non-pharmacological therapies and strategies

INITIAL CONTROLLER TREATMENT

- Start controller treatment early;
  - For best outcomes, initiate controller treatment as early as possible after making the diagnosis of asthma because delayed initiation decreases lung function.
  - All adults and adolescents with asthma should receive ICS-containing controller treatment to reduce their risk of serious exacerbations and to control symptoms.

  - For safety, treatment of asthma in adults and adolescent with SABA alone is no longer recommended.

- For patients presenting with mild symptoms (asthma symptoms or need for reliever twice a month or more), treatment with regular low-dose ICS, with SABA is highly effective.

- Consider starting at a higher step (e.g., Medium dose ICS or Low dose ICS/LABA) if;

  - Patient has troublesome asthma symptoms on most days.

  - Waking from asthma once or more a week, especially if any risk factors for exacerbations.

- If initial asthma presentation is with Severely uncontrolled asthma or an exacerbation;

  - Give a short course of oral corticosteroids (OCS) and start regular controller treatment (e.g. high dose ICS or medium dose ICS/LABA, then step down after 3 months when well controlled).

INITIATION AND MONITORING OF CONTROLLER TREATMENT

- Before starting initial controller treatment;

  - Record evidence for diagnosis of asthma, if possible.

  - Record symptom control and risk factors, including lung function.

  - Consider factors affecting choice of treatment for this patient.

  - Ensure that the patient can use the inhaler correctly.

  - Schedule an appointment for a follow-up visit.

- After starting initial controller treatment;

  - Review response after 2-3 months, or according to clinical urgency.

  - Adjust treatment (including non-pharmacological treatments).

  - Consider stepping down when asthma has been well-controlled for 3 months.

Presenting symptoms	Asthma symptoms up to 2 times per month (Mild asthma), GINA step 1 & 2	Troublesome asthma symptoms most days (Moderate asthma) GINA step 3	Severe uncontrolled asthma GINA step 4 & 5
Treatment	Step GREEN(G) (Use 1 or more controller medication)	Step YELLOW (Y) (Use 2 or more controller medications)	Step RED (R) (Use 3 or more controller medications)
	Daily Low dose ICS with as-needed SABA	Medium dose ICS with as-needed SABA	High dose ICS with as-needed SABA (concomitantly use 1 or 2 of the add on therapy)
	Low dose ICS taken whenever SABA is taken	Low dose ICS-LABA as maintenance and reliever therapy with ICS-formoterol	Daily medium to high dose ICS-LABA, with as-needed SABA Add on tiotropium
	As-needed low dose ICS-formoterol (Budesonide-formoterol)	Low dose ICS-LABA, with as-needed SABA	Medium to high dose ICS-LABA with as-needed SABA Add on LTRA
	Daily LTRA, with as-needed SABA	Low dose ICS with daily LTRA, with as-needed SABA	Medium to high dose ICS-LABA with as-needed SABA Add on Theophylline sustained-release preparation
		Low dose ICS with daily Theophylline sustained-release preparation, with as-needed SABA	Medium to high dose ICS-LABA with as-needed SABA Any of the add on drugs Add on low dose OCS Add on azithromycin

Figure 14.1: Stepwise approach to asthma therapy according to the severity of asthma and ability to control symptoms *(adopted from the Ethiopian Asthma and COPD management guideline, 2020)*

NOTES ON STEPWISE APPROACH TO ASTHMA THERAPY

- Provide guided self-management education
- Treat modifiable risk factors and comorbidities
- Advise about non-pharmacological therapies and strategies
- Consider stepping up if … uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique and adherence first.
- Consider stepping down if … symptoms controlled for 3 months + low risk for exacerbations. Stopping ICS is not advised in adults with asthma because of risk of exacerbations

ASSESSING ASTHMA SEVERITY

- How do you assess Asthma severity?
    - Asthma severity is assessed retrospectively from the level of treatment required to control symptoms and exacerbations
- When do you assess Asthma Severity?
    - Assess asthma severity after patient has been on controller treatment for several months
    - Severity is not static it may change over months or years, or as different treatments become available
- Categories of asthma severity.
    - *Mild asthma:* well-controlled with GINA Steps 1 or 2 or step G (low dose ICS, with as-needed SABA)
    - *Moderate asthma:* well-controlled with GINA Step 3 or step Y (low-dose ICS/LABA)
    - *Severe asthma:* requires GINA Step 4/5 or step R (moderate or high dose ICS/LABA ± add-on), or remains uncontrolled despite this treatment. It may appear similar to asthma that is uncontrolled due to lack of treatment.

REVIEWING RESPONSE AND ADJUSTING TREATMENT

- How often should asthma be reviewed?
    - 1-3 months after treatment started, then every 3-12 months.
    - During pregnancy, every 4-6 weeks.
    - After an exacerbation, within 1 week.
- Stepping up asthma treatment;
    - Sustained step-up, for at least 2-3 months if asthma poorly controlled;
        - Important: first check for common causes (symptoms not due to asthma, incorrect inhaler technique, poor adherence, persistent environmental exposures and drugs, comorbidities that may contribute to respiratory symptoms).
    - Short-term step-up, for 1-2 weeks, e.g. with viral infection or allergen;
        - May be initiated by patient with written asthma action plan.
    - Day-to-day adjustment;
        - For patients prescribed low-dose ICS/formoterol maintenance and reliever regimen*
- Stepping down asthma treatment;
    - Consider step-down after good control maintained for 3 months.
    - Find each patient's minimum effective dose that controls both symptoms and exacerbations.

TREATING MODIFIABLE RISK FACTORS

- Exacerbation risk can be minimized by optimizing asthma medications, and by identifying and treating modifiable risk factors.
- Provide skills and support for guided asthma self-management
    - This comprises self-monitoring of symptoms and/or PEF, a written asthma action plan and regular medical review.

  - Encourage adherence to medications and appointments
  - Give asthma information
- Prescribe medications or regimen that minimizes exacerbations
  - ICS-containing controller medications reduce risk of exacerbations
  - For patients with ≥1 exacerbation in the last year, consider low-dose ICS/formoterol maintenance and reliever regimen*
- Encourage avoidance of tobacco smoke (active or environmental tobacco smoke (ETS))
  - Provide smoking cessation advice and resources at every visit
- For patients with severe asthma
  - Refer to a specialist center, if available, for consideration of add-on medications and/or sputum-guided treatment
- For patients with confirmed food allergy:
  - Appropriate food avoidance
  - Ensure availability of injectable epinephrine for anaphylaxis

NON-PHARMACOLOGICAL STRATEGIES AND INTERVENTIONS

- Reduce indoor air pollution by cooking outside or using smokeless cooking stoves
- Avoid allergens that the patient is sensitive to:
  - contact with furry animals (e.g. cats, dogs)
  - Reduce pollen exposure
  - Reduce exposure to house dust mite
- Avoidance of tobacco smoke exposure
  - Provide advice and resources at every visit; advise against exposure of children to ETS (house, car).

- Occupational asthma
    - Ask patients with adult-onset asthma about work history. Remove sensitizers and irritants like dust and fumes as soon as possible. Refer for expert advice, if available.
- Encourage Physical activity
    - Encouraged because of its general health benefits. Provide advice about managing exercise-induced bronchoconstriction.
- Avoid medications that may worsen asthma
    - Always ask about asthma before prescribing NSAIDs or beta-blockers.
- Remediation of dampness or mold in homes
    - Reduces asthma symptoms and medication use in adults.

PATIENTS WITH POOR ASTHMA CONTROL SHOULD BE ASSESSED FOR THE FOLLOWING:

- Reasons for poor adherence and misunderstanding the difference between relievers and controllers
- Poor inhaler technique
- Exposure to trigger factors at home and work
- Presence of gastro-esophageal acid reflux disease (GERD)
- Rhinitis and sinusitis
- Use of medications that may aggravate asthma such as aspirin, non-steroidal
- anti-inflammatory drugs and ß blockers
- Other medical conditions mimicking asthma symptoms (e.g. cardiac disease).

INDICATIONS FOR CONSIDERING REFERRAL

- Difficulty confirming the diagnosis of asthma
- Suspected occupational asthma

- Persistent uncontrolled asthma or frequent exacerbations
- Risk factors for asthma-related death
- Significant side-effects (or risk of side-effects)
- Symptoms suggesting complications or sub-types of asthma
- Asthma with confirmed food allergy.

ASTHMA EDUCATION

Goals of asthma education include:

- An explanation of the nature of asthma and its inflammatory basis
- A description of the different classes of drugs and their purpose in treatment (i.e. as-needed "relievers" and regular "controllers")
- Advice on prevention strategies (allergen, irritant, and tobacco smoke avoidance)
- The correct choice and use of inhalers and the opportunity to practice under supervision
- How to recognize worsening asthma and how and when to implement their action plan
- In some patients, particularly those requiring stabilization or patients who have had a recent exacerbation or deterioration, the use of a PEF meter and chart.

ASTHMA MEDICATIONS AND COMMON SIDE EFFECTS

- Asthma medications can be divided into two categories, quick-relief and long-term control medications
- Quick-relief medications that act principally by direct relaxation of bronchial smooth muscle, thereby promoting prompt reversal of acute airflow obstruction to relieve accompanying symptom.
    - Short acting beta agonists (SABA) are the main stay of treatment.
    - SABAs are the most effective bronchodilators during exacerbations and provide immediate relief of symptoms.

- Salbutamol (Albuterol) Inhaler is available in Ethiopia.
- Regularly scheduled use is not generally recommended.
- SABA alone therapy is no longer recommended. Common but benign side effects include tremor and tachycardia

- Long-term control (controller) medications that act primarily to attenuate airway inflammation and that are taken daily independent of symptoms to achieve and maintain control of persistent asthma.
- Steroids (ICS or OCS), long-acting beta agonists (LABA), and leukotriene modifiers comprise the important long-term control medications.
- LABAs provide bronchodilation for up to 12 hours after a single dose.
    - Salmeterol and formoterol are the LABAs available for asthma.
    - LABAs should not be used as monotherapy since they have no anti-inflammatory effect, use with inhaled corticosteroids.
    - They should not be used for symptom relief or exacerbations.
- Corticosteroids are the most potent and consistently effective anti-inflammatory agents currently available.
    - They decrease both acute and chronic inflammation, resulting in reduced symptoms and improved lung function.
    - These agents may also potentiate the action of beta-adrenergic agonists.
    - ICS (See tables 14.2 below) and OCS (prednisolone 5mg tabs) are used for asthma treatment.
    - Inhaled corticosteroids are preferred, first-line agents for all patients with persistent asthma.
    - Patients with persistent symptoms or asthma exacerbations who are not taking an inhaled corticosteroid should be started on one.
    - Inhaled corticosteroids have few side effects at standard treatment doses.
    - Some of the local side effects include oral candidiasis, dysphonia, reflex

cough and bronchospasm.

  - High dose ICS and long-term use of oral steroids predisposes to systemic side effects which includes adrenal suppression, osteoporosis, skin thinning, easy bruising, diabetes, hypertension, infections, glaucoma and cataracts.

- Theophylline provides mild bronchodilation in asthmatic patients.
  - Theophylline also has anti-inflammatory and immunomodulatory properties, enhances mucociliary clearance, and strengthens diaphragmatic contractility.
  - Sustained-release theophylline preparations (e.g., theophedrine 120/11mg tablets 1-4 times per day) are effective in controlling nocturnal symptoms
  - As an added therapy in patients with moderate or severe persistent asthma whose symptoms are inadequately controlled by inhaled corticosteroids.
  - When added to an inhaled corticosteroid, theophylline may allow equivalent control at lower corticosteroid doses.
  - Theophylline use needs to be monitored closely owing to the medication's narrow therapeutic-toxic range, individual differences in metabolism, and the effects of many factors on drug absorption and metabolism.
  - At therapeutic doses, potential adverse effects include insomnia, aggravation of dyspepsia and gastroesophageal reflux, and urination difficulties in men with prostatic hyperplasia.
  - Dose-related toxicities include nausea, vomiting, tachyarrhythmias, headache, seizures, hyperglycemia, and hypokalemia.
- Leukotriene receptor antagonists (LTRA) are less effective than ICS particularly for exacerbations.
  - They may be appropriate for initial controller treatment for some patients who are unable or unwilling to use ICS; for patients who experience intolerable side-effects from ICS; or for patients with

concomitant allergic rhinitis.

- ○ Before prescribing montelukast (adult dose 10 mg once daily), health professionals should counsel patients about the risk of neuropsychiatric events.
- ○ Add-on tiotropium (long-acting muscarinic antagonist) in patients whose asthma is not well controlled with ICS-LABA.
- ○ It (mostly 5 μg once daily by mist inhaler) modestly improves lung function and modestly increases the time to severe exacerbation requiring oral corticosteroids.
- ○ Add-on azithromycin (three times a week) for adult patients with persistent symptomatic asthma despite moderate-high dose ICS and LABA reduced asthma exacerbations.
- ○ Common side effects include diarrhea, ototoxicity and cardiac arrhythmia.
- ○ Before considering add-on therapy with azithromycin, ECG should be checked for long QTc.

Table 14.2: Inhaled corticosteroids (ICS) and Combinations for Adults and adolescents (≥12 years) (Adopted from the Ethiopian Bronchial asthma and COPD management guideline, 2020)

Inhaled corticosteroid	**Total daily dose (mcg)**		
	Low	**Medium**	**High**
Beclomethasone dipropionate (CFC)	200–500	500–1000	>1000
Beclomethasone dipropionate (HFA)	100–200	200–400	>400
Budesonide (DPI)	200–400	400–800	>800
Fluticasone propionate (DPI or HFA)	100–250	250–500	>500
Fluticasone/salmeterol (DPI)	100/50	250/50	500/50
Budesonide/formoterol*(HFApMDI)	80/4.5	160/4.5	320/9
Mometasone furoate (HFA-pMDI)	200-400		>400

NB: DPI-Dry Powder inhaler, MDI -Metered dose inhaler CFC-Chloroflourocarbon HFA-Hydroflouroalkane

*When Budesonide/formoterol is prescribed as maintenance and reliever therapy, the maximum recommended dose of formoterol in a single day is 72 mcg.

HOW TO USE INHALERS FOR ASTHMA MANAGEMENT

- An inhaler is a medical device used for delivering medication into the body via the lungs.
- It is mainly used in the treatment of asthma and chronic obstructive pulmonary disease.
- The two most common forms are: metered-dose inhaler; dry powder inhalers
- Some of the types of inhalers include: Auto halers (Breath Activated aerosol devices), Nebulizers mists and nasal inhalers
- Most patients (up to 80%) cannot use their inhaler correctly. This contributes to poor symptom control and exacerbations.
- To ensure effective inhaler use:
    - Choose the most appropriate device for the patient before prescribing
    - Check in haler technique at every opportunity
    - Correct using physical demonstrations
    - Paying attention to incorrect steps and
    - Confirm that you have checklists.

METERED-DOSE INHALER (MDIS)

- The medicine is in a small canister, inside a plastic case. When the inhaler is pressed, a measured dose of medicine comes through the mouthpiece.
- MDIs require good technique and coordination by pressing down on the inhaler and breathing in at the same time.

- Because using the inhaler correctly can be difficult, spacer devices are recommended for use with MDIs.
- The spacer is attached to the MDI to make it easier to use the inhaler and get more medicine into the lungs.

HOW TO USE METERED DOSE INHALER

- Remove the cap and check the mouthpiece is clean and free of objects.
- Shake the inhaler four or five times.
- Holding the inhaler upright with your thumb on the base, breathe out as far as comfortable
- Place the mouthpiece in your mouth closing your lips around it to form a good seal, do not bite.
- Start to breathe in slowly; press down firmly on the top of the canister to release a dose; while continuing to breathe in slowly and deeply.
- Removing the inhaler from your mouth; hold your breath for about 10 seconds, or as long as is comfortable.
- Breathe out gently away from your inhaler mouthpiece
- For a second dose, wait approximately 30 seconds before repeating steps
- Replace the cap

Figure 14.2: Metered Dose Inhaler *(Adopted from the Ethiopian Bronchial asthma and COPD management guideline)*

DRY POWDER INHALER (DPI)

- Dry powder inhalers are handheld devices that deliver medication to the lungs and airways as you inhale through it.
- Examples of dry powder inhalers include: Turbuhaler; Accuhaler; Handihaler; Ellipta inhaler and Breezhaler.
- The common forms available in Ethiopia are Turbuhaler (eg.Symbicort) and Accuhaler (eg. Seritide)

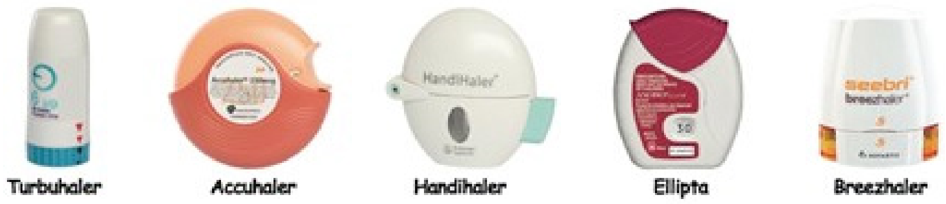


Figure 14.3: Different forms of devices delivering DPIs (Adopted from the Ethiopian Bronchial asthma and COPD management guideline, 2020)

HOW TO USE ACCUHALER® (DRY POWDER INHALER-DPI)

- Check dose counter.
- Open cover (Use thumb grip)
- Hold the casing of the Accuhaler® in one hand while sliding the thumb grip away until a click is heard
- Holding your Accuhaler® with the mouthpiece towards you slide the lever away from you until a click is heard. This makes the dose available for inhalation and moves the dose counter on.
- Holding the inhaler horizontally, breathe out as far as comfortable
- Place the mouthpiece in your mouth; closing your lips around it to form a good seal - do not bite

- Breathe in as strongly and deeply as possible
- Removing the inhaler from your mouth; hold your breath for about 10 seconds, or as long as is comfortable
- Breathe out gently away from your inhaler mouthpiece
- To close the Accuhaler®, slide the thumb grip back towards you as far as it will go until it clicks.

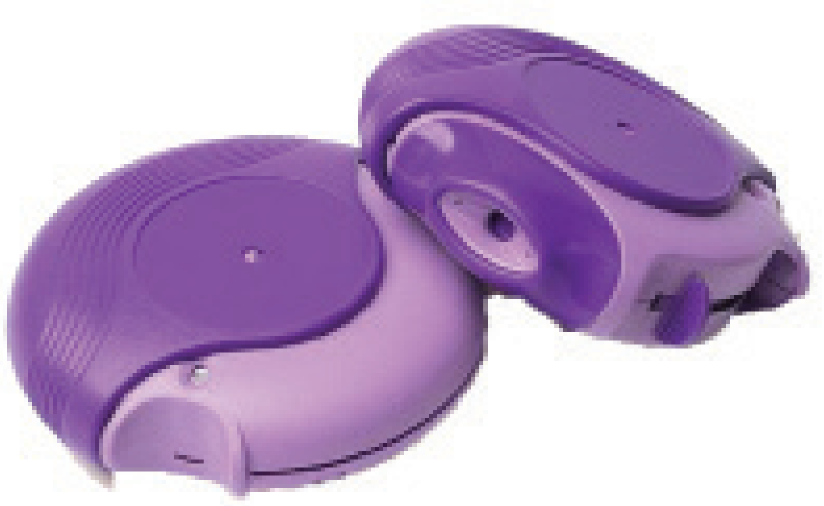


Figure 14.4: Dry Powder Inhaler (Accuhaler) (Adopted from the Ethiopian Bronchial asthma and COPD management guideline, 2020)

TURBUHALER (DPI)

- Since the turbuhaler is a breath-activated device, to use the turbuhaler properly, you must be able to breathe in deeply.
- Adults and children 7 years of age and older should be able to use the turbuhaler.

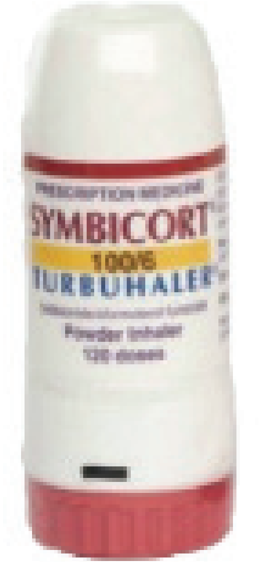


Figure 14.5: Dry Powder Inhaler (Turbuhaler) (Adopted from the Ethiopian Bronchial asthma and COPD management guideline, 2020)

HOW TO USE TURBUHALER (DPIS)

- Open by unscrew and remove the cap.
- Hold the turbuhaler upright
- Load the dose: twist the base anticlockwise and then back in the other direction until you hear a click. Your turbuhaler is now loaded with one dose of medicine
- Breathe out, away from the turbuhaler, do not blow directly into the turbuhaler
- Place the mouth piece in your mouth and form a seal with your lips and breathe in deeply.
- Remove the turbuhaler and hold your breath for up to 10 seconds.
- To close, replace the cap and twist until it is on properly.
- Cleaning and storing your turbuhaler: wipe the mouthpiece with a clean dry tissue.

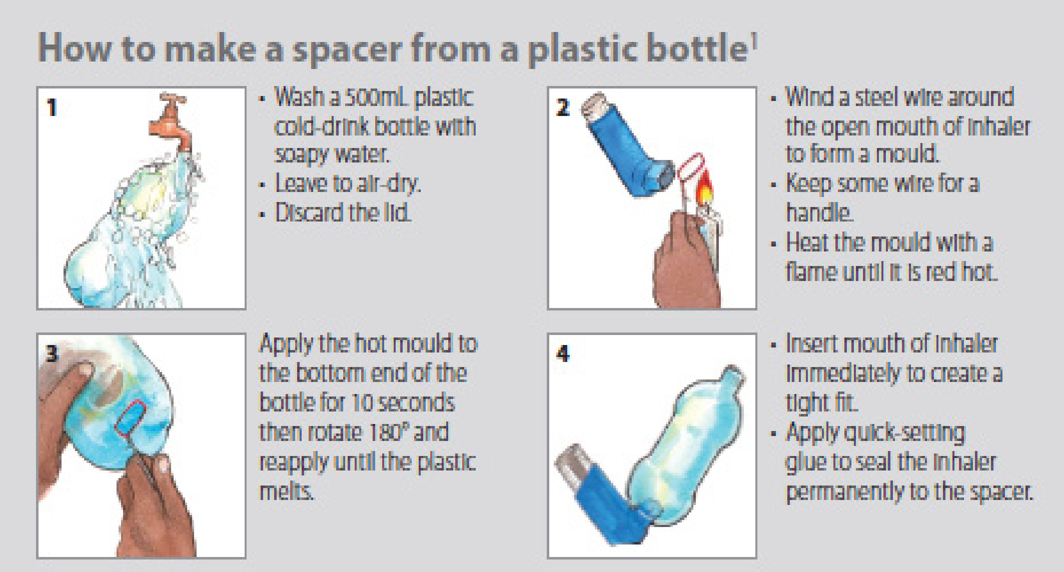
- Do not wash or allow the mouthpiece it to get wet when cleaning.
- Keep the cap on when not in use.
- The device may clog if exhaled or dribbled into or if stored in an area of high humidity with the cap off or unsealed.

COMMON PROBLEMS WHEN USING A TURBUHALER

- To get the most benefit, it is important to use the correct technique.
- Here are a few common problems:
  - Not holding your turbuhaler upright (vertical) while loading the dose.
  - Covering the air inlets with your lips.
  - Breathing in through your nose instead of your mouth.
  - Shaking the inhaler to see how much is left.
  - Storing your turbuhaler in a damp place with the cap off.

HOW TO USE SPACERS

- If patient unable to use an inhaler correctly, add a spacer to increase drug delivery to the lungs, especially if using inhaled corticosteroids. This may also reduce the risk of oral candida.
- Clean the spacer before first use and every second week: remove the canister and wash spacer with soapy water. Allow it to drip dry. Avoid rinsing with water after each use.
- Spacers are not commonly available in Ethiopia so a plastic water bottle. See figure 14.6 below to modify a 500ml plastic bottle for use as an effective spacer



How to make a spacer from a plastic bottle[1]

1
- Wash a 500mL plastic cold-drink bottle with soapy water.
- Leave to air-dry.
- Discard the lid.

2
- Wind a steel wire around the open mouth of inhaler to form a mould.
- Keep some wire for a handle.
- Heat the mould with a flame until it is red hot.

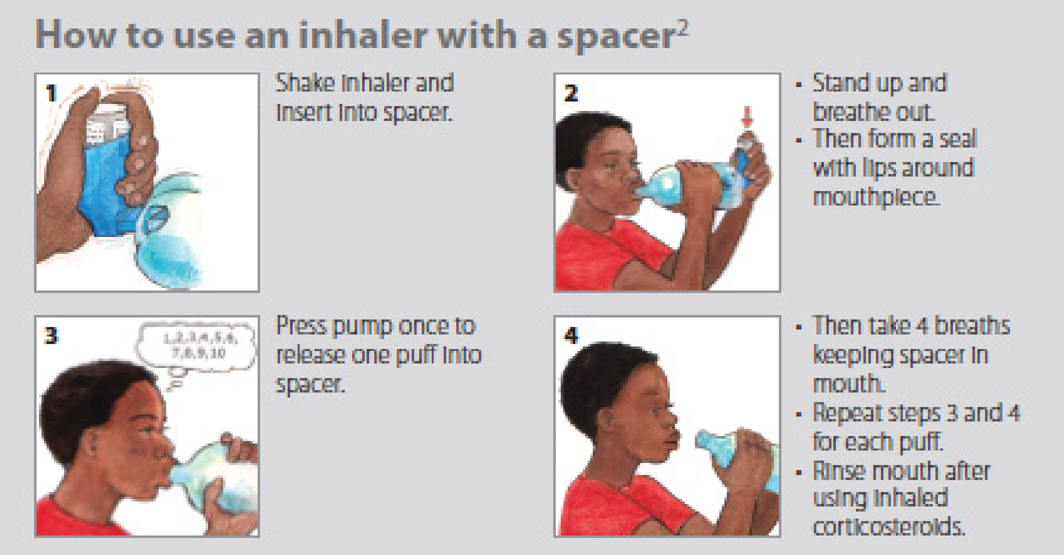
3
Apply the hot mould to the bottom end of the bottle for 10 seconds then rotate 180° and reapply until the plastic melts.

4
- Insert mouth of inhaler immediately to create a tight fit.
- Apply quick-setting glue to seal the inhaler permanently to the spacer.

Figure 14.6: How to make a spacer from a plastic bottle (Adopted from the Ethiopian Bronchial asthma and COPD management guideline, 2020)

How to use a bottle spacer

- Use a modified 500ml plastic bottle in a similar way to a conventional spacer



How to use an inhaler with a spacer[2]

1
Shake inhaler and insert into spacer.

2
- Stand up and breathe out.
- Then form a seal with lips around mouthpiece.

3
Press pump once to release one puff into spacer.

4
- Then take 4 breaths keeping spacer in mouth.
- Repeat steps 3 and 4 for each puff.
- Rinse mouth after using inhaled corticosteroids.

Figure 14.7: How to use an inhaler with a spacer (Adopted from the Ethiopian Bronchial asthma and COPD management guideline, 2020)

FURTHER READING

1. Ethiopian Bronchial asthma and COPD management guideline, 2020
2. Guideline for the Asthma management and prevention; Global Initiative for Asthma, 2020

CHRONIC OBSTRUCTIVE PULMONARY DISEASES (COPD)

BRIEF DESCRIPTION

- Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease
- It is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

CLINICAL FEATURES

- Chronic and progressive dyspnea
- Cough
- Sputum production
- Wheezing and chest tightness
- Others – including fatigue, weight loss, anorexia, syncope, rib fractures, ankle swelling, depression, anxiety.
- Chest auscultation may demonstrate bilateral wheeze or crackles.

DIAGNOSIS

- The diagnosis of COPD is based on signs and symptoms and is confirmed by spirometry.
- Spirometry is required to make the diagnosis of COPD
- The presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation.

- However, spirometry is often not available hence clinical criteria can be used to determine probability of COPD.
- COPD should be considered in any patient over the age of 40 years who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.
- Other diagnostic tests can be employed to rule out concomitant disease or tailor additional treatment
    - CXR, CBC to exclude anemia or polycythemia
    - ECG and echocardiography in patients with signs of cor pulmonale
- Pulse oximetry at rest, with exertion, and during sleep should be performed to evaluate for hypoxemia and the need for supplemental oxygen.

MANAGEMENT OF COPD

An effective COPD management plan includes four components:

- Assess and monitor disease
- Reduce risk factors
- Manage stable COPD
- Manage exacerbations

The goals of effective COPD management are to:

- Prevent disease progression
- Relieve symptoms
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

MANAGEMENT OF STABLE COPD

- The management of stable COPD focuses on improving breathlessness, reducing the frequency and the severity of exacerbations, and improving health status and prognosis.
- It includes avoidance of modifiable risk factors, vaccinations, pharmacologic therapies, oxygen therapy and pulmonary rehabilitation.
- Avoidance of modifiable risk factors: smoking cessation and reduction of indoor air pollution.
  - Smoking cessation: This is a known to affect the natural course of COPD and should be advised to all patients irrespective of the level of symptom control or severity of disease. For details on smoking cessation, see the session under "COPD Prevention" below.
  - Reduction of indoor air pollution through introduction of non-smoking cooking devices or alternative fuels should be encouraged.
- Vaccinations:
  - Influenza vaccination reduces serious illness and death.
  - It is recommended for all patients with COPD.
  - Pneumococcal vaccination (PCV13 and PPSV23) is recommended for all patients ≥65.
  - The PPSV23 is also recommended in younger patients with significant comorbidity including chronic lung or heart diseases.
- Pharmacological therapies: These are used to reduced symptoms, reduce the frequency and severity of exacerbations, and improve exercise tolerance and health status.
  - Beta-2 agonists:
    - Short-acting bronchodilators (SABA) like Salbutamol may be used for patients with mild disease
    - Longer-acting bronchodilators (LABA) like Salmeterol and

Formoterol inhalers are usually more appropriate for those with moderate to severe disease.

  - Regular and as needed SABAs improves symptoms and FEV1.
  - The effect of SABAs usually wears off in 4 – 6 hours whereas those LABAs have duration of action up to 12 hours.
  - SABAs can also be used as needed (in between doses of LABAs). Important side effects include tachycardia and somatic tremor.

- Antimuscarinic (Anticholinergic) drugs:
  - These include the Short Acting Muscarinic Antagonist (SAMA) like Ipratropium and the Long-Acting Muscarinic Antagonist (LAMA) like Titropium.
  - Ipratropium has a duration of action that is between 6 – 8 hours whereas Tiotropium lasts for up to 24 hours.
  - LAMAs generally improve symptoms and health status, and reduce exacerbations and related hospitalizations.
  - Dryness of the mouth is the most important side effect of these drugs.
- Oral bronchodilator therapy:
  - Methylxanthines (theophedrine) may be contemplated in patients who cannot use inhaled devices efficiently.
  - Side effects include palpitations caused by atrial and ventricular arrhythmias, grand mal convulsions, headaches, insomnia, nausea, and heartburn.
- Combined inhaled glucocorticoids and bronchodilators:
  - The fixed combination of an inhaled glucocorticoid and a LABA (e.g. fluticasone with salmeterol, budesonide with formoterol)
  - It improves lung function, reduces the frequency and severity of exacerbations and improves quality of life especially in patients with moderate to very severe COPD and exacerbations.

  - These advantages may be accompanied by an increased risk of pneumonia, particularly in the elderly.
  - Use this combination especially when there is history of hospitalization for exacerbation, two or more exacerbations per year, blood eosinophils >300/micL or history of (concomitant) asthma.
  - Because there is no loose preparation of LABAs in the market, we generally tend to use combination of LABA/ICS.
- Oral glucocorticoids:
  - Oral glucocorticoids are useful during exacerbations but maintenance therapy contributes to osteoporosis and impaired skeletal muscle function, and should be avoided.
  - Oral glucocorticoid trials assist in the diagnosis of asthma but do not predict response to inhaled glucocorticoids in COPD.

- Pulmonary rehabilitation:
  - Exercise should be encouraged at all stages and patients reassured that breathlessness, while distressing, is not dangerous.
  - Physical training, disease education and nutritional counseling reduce symptoms, improve health status and enhance confidence.
- Oxygen:
  - The long-term administration of oxygen (>15hrs/day) to patients with severe resting hypoxemia increases survival.
  - It is indicated for patients with a PaO2 <55mmHg or SaO2 <88% confirmed twice over three-weeks period
  - It is also indicated for patients with PaO2 55 – 60mmHg or SaO2 <88% if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive heart failure or polycythemia (Hct >55%).

MANAGEMENT OF EXACERBATION OF COPD

- Most COPD patients in our country are undiagnosed, a few of them are told they have "bronchitis" without confirmatory spirometry and still fewer have confirmed COPD.

- Therefore, COPD with acute exacerbation should be considered in every patient presenting with a recent worsening of his/her long standing cough or dyspnea or sputum color change (purulence).
- COPD exacerbations can be classified into 4 categories based on severity
    - Mild: can be managed at home with SABAs only.
    - Moderate: can be managed as outpatient with SABAs + antibiotics+ steroids.
    - Severe without respiratory failure: can be treated in the wards with SABAs + antibiotics+ steroids.
    - Severe with respiratory failure: Needs ICU admission for respiratory support (Noninvasive or invasive ventilation).

PHARMACOLOGIC MANAGEMENT INCLUDES:

- Bronchodilators
    - Short acting bronchodilators:
        - Metered dose inhaler (MDI)= Salbutamol inhaler: 2-3 puffs every hour and then tapered to 2 puffs every 4hrs.
        - Nebulization of salbutamol or combined salbutamol/ipratropium bromide solution.
    - Long-acting bronchodilators + ICS: should be continued if patient was using them and should be started at discharge if they were not being used.
- Corticosteroids
    - Only used when having a significant exacerbation (moderate or severe disease), as they may lead to development of pneumonia and sepsis
    - Can be given orally (prednisolone 40mg) or IV (hydrocortisone or methylprednisolone)

ORAL AND IV ROUTES ARE EQUALLY EFFECTIVE

  - o Recommended for 5-7days only

- Antibiotics
  - o Recommended for moderate to severe illness or when the sputum is purulent.
  - o Antibiotics are usually given for 5-7days
  - o The specific antibiotic given should depend on the sensitivity pattern of the hospital.
  - o Commonly Amoxiciline/clavulanic acid, cefalosporins, quinolones or macrolids can be used.
  - o Sputum culture is generally not helpful except in few conditions which may be associated with Gram negative infections like pseudomonas earoginosa.
    - Patient has recurrent exacerbation.
    - Patient is on invasive mechanical ventilation.
- Oxygen therapy
  - o Delivers a flow rate of <15L/min.
  - o Source of oxygen can be a cylinder (>99% pure oxygen) or oxygen concentrator (90% oxygen,10% nitrogen).
  - o Titrated to achieve a saturation of oxygen of 88-90% to avoid oxygen induced hypercapnia.

REFERRAL

  - o Patients who need further therapy and optimization
  - o Those requiring
    - High flow oxygen
    - Non-invasive ventilation: BIPAP devices
    - Invasive Mechanical ventilation

FURTHER READING

1. Ethiopian Bronchial asthma and COPD management guideline, 2020

14.3 PNEUMONIA

- For the following topics see the "pulmonary infections" section of the infectious disease chapter (Chapter 7)
    - Community Acquired Pneumonia (CAP)
    - Hospital-Acquired and Ventilator-Associated Pneumonia
    - Empyema and Complicated Parapneumonic Effusions
    - Aspiration Pneumonia and Lung Abscess

14.4 BRONCHIECTASIS

BRIEF DESCRIPTION

- Bronchiectasis is permanent, abnormal dilation and destruction of bronchial walls with chronic inflammation, airway collapse, and ciliary loss/dysfunction leading to impaired clearance of secretions.

CAUSES

- Post TB fibrosis is the commonest cause in Ethiopia.
- Recurrent infections (airway obstruction, immunodeficiency, allergic bronchopulmonary aspergillosis, mycobacterium)
- Cystic fibrosis (CF) is the most common cause of bronchiectasis (accounts for half of all cases)
- Primary ciliary dyskinesia (e.g., Kartagener syndrome)
- Autoimmune disease (rheumatoid arthritis, systemic lupus erythematosus, Crohn disease, etc.)
- Humoral immunodeficiency (abnormal lung defense), airway obstruction

- A variety of infections can cause bronchiectasis by destroying and damaging the bronchial walls and interfering with ciliary action.

CLINICAL FEATURES

- Chronic cough with large amounts of mucopurulent, foul-smelling sputum
- Dyspnea
- Hemoptysis—due to rupture of blood vessels near bronchial wall surfaces; usually mild and self-limited, but sometimes can be brisk and presents as an emergency
- Recurrent or persistent pneumonia

DIAGNOSIS

- High-resolution CT scan is the diagnostic study of choice.
- PFTs reveal an obstructive pattern.
- CXR is abnormal in most cases, but findings are nonspecific.
- Bronchoscopy may be helpful for infectious workup.

TREATMENT

- Antibiotics for acute exacerbations—superimposed infections are signaled by change in quality/quantity of sputum, fever, chest pain, etc.
- Bronchial hygiene is very important.
- Hydration
- Chest physiotherapy (postural drainage, chest percussion) to help remove the mucus
- Inhaled bronchodilators
- Consider steroid
- Refer patients to specialist for better evaluation
- The main goal in treating bronchiectasis is to prevent the complications of pneumonia and hemoptysis.

FURTHER READING

1. Steven Agabegi, Elizabeth Agabegi. Step-Up to Medicine. 5th edition, 2020

CHAPTER 15:

EMERGENCY CONDITIONS

15.1 TRIAGE IN THE EMERGENCY DEPARTMENT

- Emergency department triage is the process of quickly sorting patients to determine priority of further evaluation of care at the time of patient arrival in the emergency department, that is, to sort and assign the right patient to the right resources in the right place at the right time.
- Triage is not an endpoint but the beginning of the medical screening examination process.
- Whenever there is a crowding that occurs daily in most emergency departments, the accuracy of the triage acuity level is even more critical.
- Under-categorization (under-triage) leaves the patient at risk for deterioration while waiting.
- Rapid and accurate triage of the patient is important for successful ED operations. This can be done using The Emergency Severity Index tool developed by joint collaboration of American College of Emergency Physicians and Emergency Nursing Association.
- The Emergency Severity Index (ESI) is a simple to use, five-level triage algorithm that categorizes emergency department patients by evaluating both patient acuity and resource needs.
- Initially, the triage team assesses only the acuity level.
- If a patient does not meet high acuity level criteria (ESI level 1 or 2), the triage team then evaluates expected resource needs to help determine a triage level (ESI level 3, 4, or 5).
- Acuity is determined by the stability of vital functions and the potential threat to life, limb, or organ.

- ESI has an algorithm that uses four decision points (A, B, C, and D) to sort patients into one of the five triage levels.
- The four decision points used in the ESI algorithm are critical to accurate and reliable application of ESI. The four decision points are reduced to four key questions:
    - A) Does this patient require immediate life-saving intervention?
    - B) Is this a patient who shouldn't wait?
    - C) How many resources will this patient need?
    - D) What are the patient's vital signs?

DECISION POINT A: DOES THE PATIENT REQUIRE IMMEDIATE LIFE-SAVING INTERVENTION?

- Simply stated, at decision point A the triage professional asks, "Does this patient require immediate lifesaving intervention?"
    - If the answer is "yes," the triage process is complete and the patient is automatically triaged as ESI level 1.
    - A "no" answer moves the user to the next step in the algorithm, decision point B.
- The following questions are used to determine whether the patient requires an immediate life-saving intervention:
    - Does this patient have a patent airway?
    - Is the patient breathing?
    - Is the health professional concerned about the pulse rate, rhythm, and quality?
    - Was this patient intubated pre-hospital because of concerns about the patient's ability to maintain a patent airway, spontaneously breathe, or maintain oxygen saturation?
    - Is the health professional concerned about this patient's ability to deliver adequate oxygen to the tissues?

  - Does the patient require an immediate medication, or other hemodynamic intervention such as volume replacement or blood?
  - Does the patient meet any of the following criteria: already intubated, apneic, pulseless, severe respiratory distress, SpO2 < 90 percent, acute mental status changes, or unresponsive?
  - Does the patient have a pulse?
  - Does the patient have chest pain with pallor, diaphoresis, acute respiratory distress or hemodynamically instability?
- The ESI level-1 patient always presents to the emergency department with an unstable condition.
- Because the patient could die without immediate care, a team response is initiated: the physician is at the bedside, and nursing is providing critical care.
- ESI level-1 patients are seen immediately because timeliness of interventions can affect morbidity and mortality.
- When determining whether the patient requires immediate life-saving intervention, the triage team must also assess the patient's level of responsiveness.
- The ESI algorithm uses the AVPU (alert, verbal, pain, unresponsive) scale. The goal for this part of the algorithm is to identify the patient who has a recent and/or sudden change in level of conscience and requires immediate intervention.
- The triage professional needs to identify patients who are non-verbal or require noxious stimuli to obtain a response.
- ESI uses the AVPU scale and patients that score a P (pain) or U (unresponsive) on the AVPU scale meet level-1 criteria.

DECISION POINT B: SHOULD THE PATIENT WAIT?

- Once the triage professional has determined that the patient does not meet the criteria for ESI level 1, the triage Professional moves to decision point B.

- At decision point B, the professional needs to decide whether this patient is a patient that should not wait to be seen.
    - If the patient should not wait, the patient is triaged as ESI level 2.
    - If the patient can wait, then the user moves to the next step in the algorithm.
- Three broad questions are used to determine whether the patient meets level-2 criteria:
    1. Is this a high-risk situation? (the one with a condition that could easily deteriorate or requiring time-sensitive treatment).
    2. Is the patient confused, lethargic or disoriented?
    3. Is the patient in severe pain or distress?
- The triaging professional obtains pertinent subjective and objective information to quickly answer these.
- ESI level-2 patients remain a high priority, and generally placement and treatment should be initiated rapidly.
    - ESI level-2 patients are very ill and at high risk.
    - The need for care is immediate and an appropriate bed needs to be found.
    - Usually, rather than move to the next patient, the triage nurse determines that the charge nurse or staff in the patient care area should be immediately alerted that they have an ESI level 2.
    - Unlike with level-1 patients, the emergency nurse can initiate care through protocols without a physician immediately at the bedside.
    - Examples of high-risk situations:
        - Active chest pain, suspicious for acute coronary syndrome but does not require an immediate life-saving intervention, stable
        - A needle stick in a health care worker
        - Signs of a stroke, but does not meet level-1 criteria

  - A rule-out ectopic pregnancy, hemodynamically stable
  - New onset of confusion in an elderly patient
  - The 3-month-old whose mother reports the child is sleeping all the time
  - The adolescent found confused and disoriented
  - A patient on chemotherapy and therefore immunocompromised, with a fever question.

DECISION POINT C: RESOURCE NEEDS

- If the answers to the questions at the first two decision points are "no," then the triage nurse moves to decision point C.
- The triage nurse should ask, "How many different resources do you think this patient is going to consume in order for the physician to reach a disposition decision?"
- The disposition decision could be to send the patient home, admit to the observation unit, admit to the hospital, or even transfer to another institution.
- This decision point again requires the triage nurse to draw from past experiences in caring for similar emergency department patients.
- ESI level 3,4 and 5 patients are prioritized based on the decision point C.

DECISION POINT D: THE PATIENT'S VITAL SIGNS

- Before assigning a patient to ESI level 3, the triaging professional needs to look at the patient's vital signs and decide whether they are outside the accepted parameters for age and are felt by the professional to be meaningful.
- If the vital signs are outside accepted parameters, the triage professional should consider upgrading the triage level to ESI level 2.
- The vital signs used are pulse, respiratory rate, and oxygen saturation and, for any child under age3, body temperature.

15.2 GENERAL APPROACHES TO EMERGENCIES

BASIC LIFE SUPPORT AND ADVANCED LIFE SUPPORT

- The actions taken during the first few minutes of an emergency are critical to victim survival.
    - IHCA and OHCA differences should be emphasized
    - **IHCA**: Early recognition and prevention → Activation of emergency response →

High quality CPR → Defibrillation → Post cardiac care → Recovery

- **OHCA**: Activation of Emergency response → High quality CPR → Defibrillation → Advanced resuscitation → Post Cardiac Care → Recovery

- Basic Life Support (BLS) defines this sequence of actions and saves lives.
- BLS includes
    - Prompt recognition and action for myocardial infarction and stroke to prevent respiratory and cardiac arrest
    - Rescue breathing for victims of respiratory arrest
    - Chest compressions and rescue breathing for victims of cardiopulmonary arrest
    - Attempted defibrillation of patients with ventricular fibrillation (VF) or ventricular tachycardia (VT) with an automated external defibrillator (AED)
    - Recognition and relief of Foreign Body Airway Obstruction
- With the inclusion of AED use in BLS skills, BLS is now defined by the first 3 links in the Chain of Survival: early access, early CPR, and early defibrillation.
- The following Adult BLS Algorithm is recommended by American Heart association for health professionals.

- Step1. Ensure scene safety
- Step 2. Check for response
- Step3. Responder should shout for nearby help. The resuscitation team can be activated before or after checking breathing and pulse.
- Step4. A check for no breathing or only gasping and a check of pulse ideally should be done simultaneously. Activation and retrieval of the AED/emergency equipment by either the lone healthcare provider or by a second person must occur immediately after the check of breathing and pulse identifies cardiac arrest.
- Step4. CPR begins immediately, and the AED/defibrillator is used if available.

The recommended CPR sequence of steps by the new guidelines is CAB (chest compressions, airway, breathing) rather than ABC (airway, breathing, chest compressions).

The AHA 2015 guideline offers the following recommendations for performance of CPR:

- Chest compressions should be performed at a rate of 100-120/min
- During manual CPR, chest compressions should be at a depth of at least 2 inches for an average adult (5 cm), while avoiding excessive chest compression depths (>2.4 inches)
- Total pre-shock and post-shock pauses in chest compressions should be as short as possible
- For adults in cardiac arrest receiving CPR without an advanced airway, it is reasonable to pause compressions for less than 10 seconds to deliver two breaths
- In adult cardiac arrest with an unprotected airway, it may be reasonable to perform CPR, in which case, the chest compression target fraction should still be as high as possible (at least 60%)
- If the patient is unresponsive with no breathing or only gasping, the patient should be assumed to be in cardiac arrest and the emergency response

system should be immediately activated.

- If a pulse is not definitely felt within 10 seconds, chest compressions should be initiated (with cycle of 30 compression and 2 breathes should be provided).
- It is reasonable for healthcare providers to provide chest compressions and ventilation for all adult patients in cardiac arrest, from either a cardiac or noncardiac cause (However, note that chest compression must pause during rhythm analysis by an AED.)
- Rapid defibrillation is the treatment of choice for ventricular fibrillation of short duration for victims of witnessed OHCA or for IHCA in a patient whose heart rhythm is monitored
- For a witnessed OHCA with a shockable rhythm, it may be reasonable for EMS systems with priority-based, multitiered response to delay positive-pressure ventilation for up to three cycles of 200 continuous compressions with passive oxygen insufflation and airway adjuncts
- Routine use of passive ventilation techniques during conventional CPR for adults is not recommended
- When the victim has an advanced airway in place during CPR, rescuers need no longer deliver cycles of 30 compressions and two breaths (i.e., interrupt compressions to deliver breaths); instead, it may be reasonable for one rescuer to deliver one breath every 6 seconds (10 breaths per minute) while another rescuer performs continuous chest compression
- For healthcare providers, if there is evidence of trauma that suggests spinal injury, a jaw thrust without head tilt should be used to open the airway.
- Holding the mask in place with the EC clamp technique and lifting the jaw to open the airway is recommended. Also Squeezing the bag for one second while watching for the rise and fall of the chest.
- During breathing and bag mask ventilation Change ventilation volumes and inspiratory times for mouth-to-mask or bag-mask ventilation as follows:
    a. Without oxygen supplement: tidal volume approximately 10 mL/kg (700 to 1000 mL) over 2 seconds

b. With oxygen supplement (≥40%): a smaller tidal volume of 6 to 7 mL/kg (approximately 400 to 600 mL) may be delivered over 1 to 2 seconds.

- Alternative airway devices (i.e., laryngeal mask airway and the esophageal-tracheal Combi tube) may be acceptable when rescuers are trained in their use.
- If an FBAO is present in a responsive adult victim, the trained rescuer should attempt to clear the airway (the Heimlich maneuver) before activating the help system.

NB: Clinicians are advised to see updated adult BLS algorithms from credible sources to facilitate the clinical care. (For instance, the 2020 "American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" can be used)

ADVANCED CARDIOVASCULAR LIFE SUPPORT (ACLS)

- Although management of cardiac arrest begins with BLS and progresses sequentially through the links of the chain of survival, there is some overlap as each stage of care progresses to the next.
- ACLS comprises the level of care between BLS and post–cardiac arrest care. The transition between basic and advanced life support should be seamless as BLS will continue during and overlap with ALS interventions.
- Advanced life support includes all the components of BLS with administration of antiarrhythmic medications, treating of reversible causes of Asystole and Pulseless electrical activity, delivering shock and advanced airway management.

NB: Clinicians are advised to see updated adult ACLS algorithms from credible sources to facilitate the clinical care. (For instance, the 2020 "American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" can be used)

CARDIAC ARREST IN PREGNANCY

- Priorities for pregnant women in cardiac arrest should include providing high quality CPR and relief of aortocaval compression with lateral uterine displacement.
- Perimortem cesarean delivery is aimed at improving maternal and neonatal

outcomes. Perimortem cesarean delivery is ideally performed within 5 minutes depending on the provider resource and skill.

- Approaches to cardiac arrest in pregnancy

  1) Continue BLS/ACLS (i) high quality CPR, ii) defibrillation if indicated, iii) other ACLS interventions (e.g. epinephrine))

  2) Organize maternal cardiac arrest team (obstetric, neonatal, emergency, anesthesiology, intensive care and cardiac arrest services)

  3) Consider etiology of arrest. Potential etiologies of maternal cardiac arrest can be easily traced as ABCDEFGH (Anesthetic complications, Bleeding, Cardiovascular, Drugs, Embolic, Fever, General non-obstetric causes of cardiac arrest, Hypertension)

  4a) Perform material interventions (i) perform airway management, ii) administer100% oxygen, avoid excess ventilation, iii) place IV above diaphragm iv) if receiving IV magnesium, stop and give calcium chloride or gluconate), Then proceed to continuous BLS/ALS back.

  4b) perform obstetric interventions (i) provide continuous lateral uterine displacement,ii) detach fetal monitors, iii) prepare for perimortem cesarean delivery) = perform perimortem cesarean delivery (if no ROSC in 5 minutes, consider immediate perimortem cesarean delivery)=transfer neonate to the neonatal team

ADVANCED AIRWAY

- In pregnancy a difficult airway is common needing the most experienced provider. Provide endotracheal intubation or supraglottic advanced airway. Preform waveform capnography or capnometry to confirm and monitor ET tube placement. Once advanced airway is in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compression.

NB: Clinicians are advised to see updated pregnant Cardiac arrest algorithms from credible sources to facilitate the clinical care. (For instance, the 2020 "American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" can be used)

I 5.3 ACUTE RESPIRATORY FAILURE

BRIEF DESCRIPTION

- Respiratory failure occurs when there is either insufficient oxygenation and/ or inadequate CO2 elimination. Broadly defined as PaO2 <50 mm Hg or PaCO2 >50 mm Hg and arterial pH <7.35 when baseline ABGs are considered normal. The PaCO2/FIO2 ratio is generally <200.
- Respiratory failure generally classified as i) hypoxemic (type I, PaO2 <60 mm Hg or low PaCO2)-Hypoxemic RF is most common type, ii) hypercapnic (type II, PaCO2 >50 mm Hg), iii) Mixed: multiple pathophysiologic processes that contribute to both hypoxemia and hypercarbia; iv) In postoperative patients with a normal respiratory pump and normal lungs who are sedated or paralyzed or when the metabolic demands are too high for the patient to compensate for it
- RF may also be classified as acute or chronic.

CLINICAL PRESENTATION

- Tachypnea, dyspnea
- Diminished breath sounds, wheezing and rhonchi, crackles
- Use of accessory muscles to breathe
- Tachycardia and cardiac arrhythmias
- Cold, clammy skin; diaphoresis
- Ashen skin
- Peripheral cyanosis of skin, oral mucosa, lips, and nailbeds
- Sitting bolt upright or slightly hunched over
- Asterixis if severe hypercapnia
- Agitation, anxiety
- Restlessness, lethargy, altered mental status (confused, disoriented), somnolence

- Seizures, coma
- Can lead to sepsis and ventilator-associated pneumonia after intubation

DIAGNOSTIC TESTS

- ABGs
- CXR and sputum cultures
- Pulmonary function tests
- CBC especially WBC, Hgb, and Hct
- ECG, echocardiogram may be helpful
- CT scan
- V/Q˙ scan
- Angiography
- Toxicology screen
- Serum chemistry tests

TREATMENT

Approach with the ABC of life. Follow primary and secondary surveys on evaluating every patient.

- Asses and maintain the airway
- Assess adequate oxygenation and ventilation status and administer O2 via mask or mechanical ventilation.
- Hemodynamic stabilization
- Assess neurologic status
- Monitor VS, heart rhythm, fluid and electrolyte balance, intake and output.
- Asses the underlying cause and treat

15.4 ALTERED MENTAL STATUS AND COMA

BRIEF DESCRIPTION

- Is a clinical state in which patients have impaired responsiveness to the external stimulation and are either difficult to arouse or are unarousable?
- Coma is defined as unarousable unresponsiveness
- Stupor, Lethargy, and Obtundation refer to the state between alertness and coma.

Generally, causes of coma are

- Drugs/Toxins
- Metabolic disorders
- Infectious or inflammatory
- Structural brain lesions
- Others; heat stroke, Non convlusive status epilpticus etc

CLINICAL FEATURES

- It should always be addressed on the Emergency bases (ABCDE). While the patient is managed with the ABCD of life, the following features can be captured to make the underling diagnosis.

History

- Ask detailed history from the family, friends, witnesses or relatives about the circumstances during and prior to altered mental state
- Ask any known medical or psychiatric condition and drug or alcohol abuse
- If available previous medical charts will help for reaching in a diagnosis

Signs

- Perform detailed physical examination including

- looking for evidences of metabolic derangements
- Detailed neurologic examination including Glasco Coma Scale, Motor and sensory examination, meningeal signs, evidences of raised ICP and herniation syndromes, cranial nerve examination

DIAGNOSIS AND INVESTIGATIONS

- The goal of diagnostic testing is to identify treatable causes for coma.
- Neurologic recovery lies on early treatment.
- Testing should be prioritized according to presentation and clinical suspicion
- Some of the investigations that should be done in accordance to clinical suspicion includes:
    - CBC
    - Organ function test including LFT and RFT
    - Serum electrolyte
    - PT, PTT, INR
    - CT scan
    - Toxicologic screen
    - Lumbar puncture and EEG based on the clinical presentation

TREATMENT

- Evaluate and resuscitate the ABC
- Take vital signs, blood for laboratory and establish the GCS
- Consider intubation for patients with GCs < 8 or frequent vomiting or poor gag or cough reflex
- Treat both hypotension and hypertension
- Give Dextrose for patients with unknown causes of coma while waiting for determination of blood glucose level and add thiamine for patients

with malnutrition or alcohol consumption, and give Naloxone for those with opioid overdose.

- If raised intracranial pressure is suspected elevate the bed to 45 degree and give mannitol (1 gm /kg IV) and/or cautiously hyperventilate patients on Mechanical ventilator
- Treat hyperthermia by efforts to lower temperature like cooling of the blanket and giving antipyretics. Also treat the underlying cause for fever
- Treat seizure with loading with phenytoin through Nasogastric tube or if IV is available by using IV phenytoin and diazepam as needed. If nonconvulsive seizure is suspected treat it as a seizure
- Establish the precise diagnosis and give the definitive treatment

15.5 ANAPHYLAXIS

BRIEF DESCRIPTION

- An acute allergic reaction or anaphylaxis is the most dramatic and severe form of immediate hypersensitivity that may cause death and requires emergent diagnosis and treatment.
- Anaphylaxis can develop within minutes of injection or ingestion of medicines or contact with trigger factors.
- Common causes are, medicines, intravenous contrast media, vaccines and antisera (e.g. TAT), insect bites, foods and additives (e.g. sea foods, nuts). But any agent capable of producing a sudden degranulation of mast cells or basophils can induce anaphylaxis including latex hypersensitivity

CLINICAL FEATURES

- Severe itching
- Urticarial rash
- Difficulty in breathing
- Collapse

- Facial edema
- Angio-edema causing difficulty in breathing due to laryngeal edema and obstruction
- Bronchospasm with wheeze
- Shock with severe hypotension
- Tachycardia
- Cyanosis

INVESTIGATION

- Diagnosis is clinical
- Clinical diagnosis of Anaphylaxis can be made if either of the three is fulfilled.

  1) Urticaria, generalized itching or flushing, or edema of lips, tongue, uvula, or skin developing over minutes to hours and associated with at least one of the following:
     - Respiratory distress or hypoxia

       or
     - Hypotension or cardiovascular collapse

       or
     - Associated symptoms of organ dysfunction (e.g., hypotonia, syncope, incontinence)
  2) Two or more signs or symptoms that occur minutes to hours after allergen exposure:
     - Skin and/or mucosal involvement
     - Respiratory compromise
     - Hypotension or associated symptoms
     - Persistent GI cramps or vomiting

3) Consider anaphylaxis when patients are exposed to a known allergen and develop hypotension

TREATMENT

OBJECTIVES

- Maintain airways, breathing and circulation
- Remove the offending cause if possible

Non pharmacologic

- **Airway:** Immediate intubation if evidence of impending (stridor's, wheezes, tachypnea and difficulty swallowing) airway obstruction from angioedema; delay may lead to complete obstruction; cricothyrotomy may be necessary
- **Oxygen:** Administer oxygen to maintain oxygen saturation above 90%
- **Circulation:** All patients with anaphylaxis should receive intravenous fluids. Some patients may require large amount of intravenous fluids due shift of intravascular fluid to the interstitial space.

○ Adults-1 to 2 liters NS fast, then depending on the patient response to adrenaline and the initial bolus of NS.

- **Position-**recumbent position, if tolerated, and elevate lower extremities
- **Remove-**the offending agent, if possible

Pharmacologic

- **Adrenaline**, IM, 0.5ml (500microgram) of 1:1000 at mid-anterolateral thigh; can repeat every 3 to 5 minutes as needed. If symptoms are not responding to epinephrine injections, prepare IV adrenaline 1 to 10 micrograms per minute by infusion; mix 1 milligram (1 mL of 1:1000 dilution) in 500 mL NS and infuse at 0.5 mL/min; titrate dose as needed

PLUS

- **Hydrocortisone**, IV, 200mg, IV, stat; then 100mg 6-8 hourly for 3 – 4 days and discontinue without tapering.

PLUS

- **Promethazine** hydrochloride, IM, 25mg 8-12 hourly or **Diphenhydramine** ,25–50 milligrams every 6 hrs. IV, IM, or PO. Then cetirizine 10mg. P.O., once/day OR Loratadine 10mg, P.O., once /day OR Chlorpheniramine 4mg, P.O., QID

  PLUS

- If wheeze develops **Salbutamol**, aerosol, 100µg/dose, 2-4 puffs every 4-6 hr.
- If the patient has concurrent use of betablocker and has refractory hypotension add glucagon 1 milligram IV every 5 min until hypotension resolves, followed by 5–15 micrograms/min infusion.

15.6 SUDDEN CARDIAC ARREST

BRIEF DESCRIPTION

- Sudden cardiac arrest (SCA) refers to the sudden cessation of cardiac activity with hemodynamic collapse, typically due to sustained ventricular tachycardia/ventricular fibrillation when the event is reversed with intervention or spontaneously; if it is not reversed it will be labeled as sudden cardiac death.
- It usually occurs in individuals with structural heart disease but in the absence of detectable clinical findings. Acute myocardial ischemia, electrolyte abnormalities, antiarrhythmic medicines and worsening Heart Failure can precipitate sudden cardiac arrest.

CLINICAL FEATURES

- Instantaneous or abrupt onset collapse with or without prodrome
- Absent pulse
- Absent or gasping type of breathing
- Unresponsive

INVESTIGATIONS

- During the episode no work up is needed except having continuous ECG monitoring together with emergency management.
- Post SCA work up is needed-Troponin, Echocardiography, Electrolytes, RFT

TREATMENT

OBJECTIVES

- Achieve adequate ventilation
- Control cardiac arrhythmia
- Stabilize blood pressure and cardiac output
- Restore organ perfusion

Non pharmacologic

- Provide Basic life support (BLS) and refer with escort

15.6 HYPOGLYCEMIA

BRIEF DESCRIPTION

- Hypoglycemia is a clinical syndrome in which low serum (or plasma) glucose concentrations leads to symptoms of sympathoadrenal activation and neuroglycopenia.
- Hypoglycemia can cause significant morbidity and may be lethal if not promptly recognized and managed.

CLINICAL FEATURES

Adrenergic symptoms:

- Sweating, sensation of warmth, anxiety, tremor or tremulousness, nausea, palpitations and tachycardia, and perhaps hunger.

Neuroglycopenic symptoms:

- Fatigue, dizziness, headache, visual disturbances, drowsiness, difficulty speaking, inability to concentrate, abnormal behavior, loss of memory, confusion, and ultimately loss of consciousness or seizures.

The presence of **Whipple's triad**

- 1. Symptoms consistent with hypoglycemia (see above)
- 2. A low blood glucose (<55mg/dl) level measured with a precise method (not a glucometer)
- 3. Relief of those symptoms after treatment the plasma glucose level is raised. In diabetic patients on insulin or insulin secretagogue plasma glucose level of 70mg/dl or less is alerting.

Hypoglycemia unawareness-absent symptoms (usually related to autonomic diabetic neuropathy)

MAJOR CAUSES OF HYPOGLYCEMIA:

- In patients with Diabetes Mellitus-Insulin and sulfonylureas excess dose or previous doses with unaccustomed exercise or omission of meals. Development of CKD, AKI, and sepsis as well.
- In non-diabetic patients with critical illnesses – Hepatic or renal failure, adrenal insufficiency, sepsis, malaria.
- Seemingly normal patients-endogenous hyperinsulinemia, accidental or surreptitious use sulfonylureas or insulin.

NB: Hypoglycemia caused by sulfonylureas can be prolonged for several days hence these patients should not be discharged with emergency room correction of hypoglycemia alone

TREATMENT

OBJECTIVES

- Quickly bring the level of blood glucose within the normal range to prevent serious brain damage.
- Maintain the level of blood glucose within the normal range until the patients begin eating normally.

Non-pharmacologic

- 2-3 teaspoons of granulated sugar or 3 cubes of sugar or 1/2 a bottle of soft drink to individuals who are conscious.

- The above measures should be followed immediately by a meal or snack.

Pharmacologic

- **Dextrose**, 40%, IV, 40-60ml over 1 to 3 minutes through a large vein, followed by 10%
- **Glucose** IV, 500ml, 4 hourly until the patient is able to eat normally.
- **Glucagon** SC/IM 1mg in adults particularly in type I DM patients.

15.7 SHOCK

15.7.1 APPROACH TO SHOCK

- Shock is a state of circulatory insufficiency that creates an imbalance between tissue oxygen supply (delivery) and oxygen demand (consumption) resulting in end-organ dysfunction.
- Reduction in effective perfusion may be due to a local or global delivery deficiency or utilization deficiency with suboptimal substrate at the cellular or subcellular level.
- The mechanisms that can result in shock are frequently divided into four categories:

  (1) Hypovolemic

  (2) Cardiogenic

  (3) Distributive

  (4) Obstructive

Table 15. 1. Types, characteristics and etiologist of shock

Type	Hemodynamic change	Etiology
Hypovolemic	Decreased preload, increased SVR, decreased Cardiac output (CO)	Hemorrhage, capillary leak, GI losses, burns
Cardiogenic	Increased preload, increased afterload, increased SVR, decreased CO	MI, dysrhythmias, heart failure, valvular disease
Obstructive	Decreased preload, increased SVR, decreased CO	PE, pericardial tamponade, tension PTX
Distributive	Decreased preload, increased SVR, Mixed CO	Sepsis, neurogenic shock, Anaphylaxis

- **Hypovolemic shock** occurs when decreased intravascular fluid or decreased blood volume causes decreased preload, stroke volume, and CO. Volume loss from different etiologies including severe blood loss (hemorrhage) can cause decreased myocardial oxygenation, which decreases contractility and CO. This action may lead to an autonomic increase in the SVR.
- In **cardiogenic shock**, the left ventricle fails to deliver oxygenated blood to peripheral tissues due to variances in contractility, as well as preload and afterload. Myocardial infarction is the most common cause of cardiogenic shock. Dysrhythmias are another common cause because they can lead to a decreased CO. Bradyarrhythmia's result in low CO, and tachyarrhythmias can result in decreased preload and stroke volume.
- **Obstructive shock** is due to a decrease in venous return or cardiac compliance due to an increased left ventricular outflow obstruction or marked preload decrease. Cardiac tamponade and tension pneumothorax are common causes.
- In **distributive shock**, there is relative intravascular volume depletion due to marked systemic vasodilatation. This is most commonly seen in septic shock. Anaphylaxis, neurogenic shock and adrenal insufficiency are additional causes of distributive shock.

PHARMACOLOGIC

15.7.2 CARDIOGENIC SHOCK (PUMP FAILURE)

First line

- **Norepinephrine (noradrenaline)**, Initial: 0.5-1 mcg/minute and titrate to desired response; 8-30 mcg/minute is usual range. Goal: MAP>65mmhg
- If myocardial infarction suspected aspirin should be loaded and immediate reperfusion.

Alternatives

- **Dopamine**, 5-20mcg/kg/min IV diluted with dextrose 5% in Water, or in sodium chloride solution 0.9%;

OR

- **Dobutamine**, 2.5-40 micrograms/kg/min IV diluted in dextrose 5%.

Never initiate Dobutamine alone in a patient with cardiogenic shock and Systolic BP< 70

OR

- **Adrenaline, I.V.** infusion: Initial: 0.1-0.5 mcg/kg/minute (7-35 mcg/minute in a 70 kg patient); titrate to desired response

15.7.3 HYPOVOLEMIC SHOCK

- **Infusion of fluid (Normal saline or Ringer lactate)** 1-2 liters fast;
- Reassess the patient for adequacy of treatment;
  - If needed repeat the bolus with maximum tolerated dose being 60 – 80 ml/kg with in the first 1 – 2 hr;
  - If needed open double IV line.
- If due to hemorrhage, apply transfusion of packed Red Blood Cells (RBC) or whole blood 20ml/kg over 4 hrs, repeat as needed until hemoglobin level reaches 10gm/dl and the vital signs are corrected.

15.7.4 SEPTIC SHOCK.

- Adequate organ system perfusion with IV fluids (large volume of IV fluids are required in septic shock patients).
- A patient with septic shock should receive initial fluid bolus of 20 mL/kg of lactated Ringers or normal saline. Repeat 2 boluses of 20ml/kg with target of SBP>90mmhg, and MAP>60mmhg. If goal not achieved, start pressors.1In general, most patients with septic shock are expected to take around 5-6 liter of IV fluids within 24 hours.
- Start Empiric therapy with broad spectrum antibiotics in septic shock patients as soon as possible at least within 01 hour of the clinical suspicion of septic shock and draw blood for culture.
- If non responsive to fluid resuscitation administer vasopressor therapy

First line

- ○ **Norepinephrine (noradrenaline),** Initial: 0.5-1mcg/minute and titrate to desired response; 8-30 mcg/minute is usual range

Alternatives

- ○ **Dopamine**, 5-50 mcg/kg/min IV diluted with dextrose 5% in Water, or in sodium chloride solution 0.9%;

  OR

- ○ **Adrenaline, I.V. infusion:** Initial: 0.1-0.5 mcg/kg/minute (7-35 mcg/minute in a70 kg patient); titrate to desired response

  OR

- If the Blood pressure doesn't respond for the initial management with vasopressors and fluids
  - ○ **Hydrocortisone**, 50 mg IV every 6 hrs (when vasopressor dependent or)

Adrenal crisis

1. Normal saline Large volumes (1 to 3 liters) or 5 % dextrose in 0.9% percent saline should be infused intravenously /infusion like hypovolemic shock.

2. **Hydrocortisone**, 200mg, IV, stat then 100mg, IV, QID
3. start the vasopressor management as a septic shock protocol if the BP doesn't respond to IV fluids and steroid therapy.

15.9 TRAUMA: GENERAL APPROACH TO TRAUMA PATIENTS

- The treatment of seriously injured patients requires the rapid assessment of injuries and institution of life-preserving therapy.
- Because timing is crucial, a systematic approach that can be rapidly and accurately applied is essential. This approach is termed the "initial assessment" and includes the following elements:
    - Triage
    - Primary survey (ABCDEs)
    - Resuscitation
    - Adjuncts to primary survey and resuscitation
    - Consideration of the need for patient transfer
    - Secondary survey (head-to-toe evaluation and patient history)
    - Adjuncts to the secondary survey
    - Continued post resuscitation monitoring and reevaluation
    - Definitive care
- The primary and secondary surveys should be repeated frequently to identify any change in the patient's status that indicates the need for additional intervention.
- Patients are assessed, and their treatment priorities are established, based on their injuries, vital signs, and the injury mechanisms.
- In severely injured patients, logical and sequential treatment priorities must be established based on overall patient assessment.

- The patient's vital functions must be assessed quickly and efficiently.
- Management consists of a rapid primary survey, resuscitation of vital functions, a more detailed secondary survey, and, finally, the initiation of definitive care.
- This process constitutes the ABCDEs of trauma care and identifies life-threatening conditions by adhering to the following sequence:
    - Airway maintenance with cervical spine protection
    - Breathing and ventilation
    - Circulation with hemorrhage control
    - Disability: Neurologic status
    - Exposure/Environmental control: Completely undress the patient, but prevent hypothermia
    - **F**: FAST (Focused Assessment of Sonography in Trauma)
- This prioritized sequence is based on the degree of life threat so that the abnormality that poses the greatest threat to life is addressed first.
- A quick assessment of the A, B, C, and D in a trauma patient can be conducted by asking the patient for his or her name, and asking what happened. Appropriate response indicates that there is no major compromise in A, B and D.

AIRWAY MAINTENANCE WITH CERVICAL SPINE PROTECTION

- Upon initial evaluation of a trauma patient, the airway should be assessed first to ascertain patency (the easiest way of assessing airway patency is asking the patient his name or get him to talk).
- This rapid assessment for signs of airway obstruction should include suctioning and inspection for foreign bodies and facial, mandibular, or tracheal/laryngeal fractures that can result in airway obstruction.
- Measures to establish a patent airway should be instituted while protecting the cervical spine (Inline stabilization). Initially, the chin-lift or jaw-thrust

maneuver is recommended to achieve airway patency. In addition, patients with severe head injuries who have an altered level of consciousness or a Glasgow Coma Scale (GCS) score of 8 or less usually require the placement of a definitive airway.

- While assessing and managing a patient's airway, great care should be taken to prevent excessive movement of the cervical spine.
- The patient's head and neck should not be hyperextended, hyper flexed, or rotated to establish and maintain the airway.
- Based on the history of a traumatic incident, loss of stability of the cervical spine should be assumed.
- Neurologic examination alone does not exclude a diagnosis of cervical spine injury. Initially, protection of the patient's spinal cord with appropriate immobilization devices should be accomplished and maintained (Cervical Collar should be applied until cervical injury is ruled out). Assume a cervical spine injury in patients with blunt multisystem trauma, especially those with an altered level of consciousness or a blunt injury above the clavicle.

BREATHING AND VENTILATION

- Airway patency alone does not ensure adequate ventilation. Respiratory rate, saturation and air entry should be checked.
- Adequate gas exchange is required to maximize oxygenation and carbon dioxide elimination.
- Ventilation requires adequate function of the lungs, chest wall, and diaphragm. Each component must be rapidly examined and evaluated.
  - The patient's neck and chest should be exposed to adequately assess jugular venous distention, position of the trachea, and chest wall excursion.
  - Auscultation should be performed to ensure gas flow in the lungs.
  - Visual inspection and palpation can detect injuries to the chest wall that may compromise ventilation.

- Injuries that severely impair ventilation in the short term include tension pneumothorax, flail chest with pulmonary contusion, massive hemothorax, and open pneumothorax.
- Appropriate measures including putting the patient on oxygen to maintain saturation, chest decompression for tension pneumothorax should be done while assessing breathing and ventilation.

CIRCULATION WITH HEMORRHAGE CONTROL

- Circulatory compromise in trauma patients can result from many different injuries.
- Hemorrhage is the predominant cause of preventable deaths after injury. Identifying and stopping hemorrhage are therefore crucial steps in the assessment and management of such patients.
- Once tension pneumothorax has been eliminated as a cause of shock, hypotension following injury must be considered to be hypovolemic in origin until proven otherwise.
- The elements of clinical observation that yield important information about the patient's hemodynamic status within seconds are level of consciousness, skin color, and pulse.
- The source of bleeding should be identified as either external or internal. External hemorrhage is identified and controlled during the primary survey. Rapid, external blood loss is managed by direct manual pressure on the wound. The major areas of internal hemorrhage are the chest, abdomen, retroperitoneum, pelvis, and long bones.
- The source of the bleeding is usually identified by physical examination and imaging (e.g., chest x-ray, pelvic x-ray, or focused assessment sonography in trauma [FAST]).
- **Management m**ay include:
  - chest decompression, pelvic binders, splint application, and surgical intervention.
  - Definitive bleeding control is essential along with appropriate replacement of intravascular volume.

- A minimum of two large-caliber intravenous (IV) catheters should be introduced.
- Blood samples taken for cross match as well.
- IV fluid therapy with crystalloids should be initiated. A bolus of 1 to 2 L of an isotonic solution may be required to achieve an appropriate response in the adult patient.
- If the patient is unresponsive to initial crystalloid therapy, blood transfusion should be given.

DISABILITY (NEUROLOGIC EVALUATION)

- A rapid neurologic evaluation is performed at the end of the primary survey.
- This neurologic evaluation establishes the patient's level of consciousness, pupillary size and reaction, lateralizing signs, and spinal cord injury level.
- The GCS is a quick, simple method for determining the level of consciousness that is predictive of patient outcome, particularly the best motor response.
- A decrease in the level of consciousness may indicate decreased cerebral oxygenation and/or perfusion, or it may be caused by direct cerebral injury.
- An altered level of consciousness indicates the need for immediate reevaluation of the patient's oxygenation, ventilation, and perfusion status.
- Hypoglycemia and alcohol, narcotics, and other drugs also can alter the patient's level of consciousness. However, if these factors are excluded, changes in the level of consciousness should be considered to be of traumatic central nervous system origin until proven otherwise.
- Primary brain injury results from the structural effect of the injury to the brain.
- Prevention of secondary brain injury by maintaining adequate oxygenation and perfusion are the main goals of initial management.

EXPOSURE AND ENVIRONMENTAL CONTROL

- **Undress**: The patient should be completely undressed, usually by cutting off his or her garments to facilitate a thorough examination and assessment.
- **Log roll:** Log roll should be done here by at least 3 health care workers two for rolling the patient and one examining. So, examiner should:
  - palpate vertebra from cervical till lumbosacral area for any tenderness or deformity,
  - check for any open wound at the back and
  - do Per Rectum examination to asses for tone and any blood on examining finger.
- **Warming:** After patient's clothing has been removed and the assessment is completed,
  - Cover patient with warm blankets or an external warming device to prevent hypothermia in the trauma receiving area.
  - Intravenous fluids should be warmed before being infused, and
  - A warm environment (i.e., room temperature) should be maintained.

ADJUNCTS TO PRIMARY SURVEY

- Adjuncts that are used during the primary survey include electrocardiographic monitoring; urinary and gastric catheters; other monitoring, such as ventilatory rate, arterial blood gas (ABG) levels, pulse oximetry, blood pressure, and x-ray examinations (e.g., chest and pelvis).

Secondary survey

- The secondary survey does not begin until the primary survey (ABCDEs) is completed, resuscitative efforts are underway, and the normalization of vital functions has been demonstrated.
- When additional personnel are available, part of the secondary survey may be conducted while the other personnel attend to the primary survey.
  - In this setting the conduction of the secondary survey should not interfere with the primary survey, which takes first priority.

- The secondary survey is a head-to-toe evaluation of the trauma patient, that is, a complete history including mechanism of injury and AMPLE history and physical examination, including reassessment of all vital signs.
    - AMPLE history stands for **A**llergies, **M**edications currently used, **P**ast illnesses/**P**regnancy, **L**ast meal, **E**vents/**E**nvironment related to the injury.
- Each region of the body is completely examined.

NB. All trauma patients should have repeated evaluations of both the primary survey and secondary survey to monitor response to interventions and to detect new abnormalities. Whenever there is a need, trauma patients should be transferred to trauma treating hospitals.

15.10 POISONING AND OVERDOSE

15.10.1 APPROACH TO A PATIENT WITH POISONING AND TOXIDROMES

- Poisoning represents the harmful effects of accidental or intentional exposure to toxic amounts of any substance. The exposure can be by ingestion, inhalation, injection, or through skin.
- The effects may occur immediately or several hours or even days after the exposure.
- The damage could be local or systemic.
- Poisoning can be from household substances (e.g. bleach), industrial (e.g. methanol), pesticides e.g. organophosphates), therapeutic medicine overdose (e.g. phenobarbitone, Amitriptyline), toxic plants (e.g. poisonous mushrooms, toxic herbal medications), bites and stings of venomous animals (e.g. snakes, bees).

Clinical features

- Clinical presentation is variable depending on the type of poison/medicine, route and dose.

- Many of the manifestation are nonspecific.
- Toxidromes are sets of clinical findings which could help in guiding the possible class of the poison/medicine
- It is very helpful to have a sample of the substance or the container in which it was stored as only few poisons can be identified instantly

Table 15.2. Toxidromes (adapted from Hand book for the Management of poisoning and overdose, Singapore MOH, 2000)

Toxidrome	Mental status	Pupil	Vital signs	Other	Examples of toxic agents
Cholinergic	Confusion Coma	Miosis	Bradycardia Hypertension or Hypotension	Salivation, urinary & fecal incontinence, diarrhea, vomiting, lacrimation, bronchoconstriction, fasciculations, weakness, seizures	Organophosphate and carbamate insecticides, nerve agents,
Anticholinergic	Agitation, hallucinations, delirium with mumbling speech, coma	Mydriasis	Hyperthermia, tachycardia, hypertension, tachypnea	Dry skin & mucous membranes, decreased bowel sounds, urinary retention, myoclonus, choreoathetosis	Antihistamines, tricyclic antidepressants, antiparkinson agents, antispasmodics, phenothiazines, atropine

Tricyclic antidepressants	Confusion, agitation, coma	Mydriasis	Hyperthermia, tachycardia, hypertension then hypotension	Seizures, myoclonus, choreoathetosis, cardiac arrhythmias	Amitriptyline, nortriptyline, imipramine,
Sedative-hypnotic	CNS depression, stupor, coma	Miosis	Hypothermia, bradycardia, hypotension, hypoventilation	Hyporeflexia	Benzodiazepines, barbiturates, alcohols,
Opioid	CNS depression, coma	Miosis	Hypothermia, bradycardia, hypotension, hypoventilation	Hyporeflexia pulmonary edema, needle marks	Opiates (eg, heroin, morphine, methadone, oxycodone)
Sympathomimetic	Hyperalert, agitation, hallucinations, paranoia	Mydriasis	Hyperthermi, tachycardia, hypertension, widened pulse pressure, tachypnea,	Diaphoresis, tremors, hyperreflexia, seizures	Cocaine, amphetamines, ephedrine, pseudoephedrine, phenylpropanolamine, theophylline, caffeine

Investigations

- Random blood sugar
- CBC
- BUN and creatinine,
- Electrolytes
- Liver function tests
- Chest X-ray for possible aspiration pneumonia
- Toxicological analysis of identified substance (e.g. Gastric aspirate) or from serum

TREATMENT

OBJECTIVES

- Maintain airway, breathing and circulation
- Reduce absorption and enhance elimination
- Antagonize or neutralize the effects
- Relieve symptoms
- Prevent organ damage or impairment

Non-pharmacologic

Supportive care

- Airway protection
- Treatment of hypoxia
- correct hypotension/arrhythmia
- Treatment of seizures
- Correction of temperature abnormalities
- Correction of metabolic derangements

PHARMACOLOGIC AND OTHER CARES

- **Prevention of further poison absorption**
    - Gastric lavage
        - Should be done within an hour of ingestion
        - Contraindicated in patients with unprotected airway, corrosive and hydrocarbon poisoning
    - Decontamination of eye
    - Skin decontamination
    - Activated charcoal
- **Enhancement of elimination**
    - Multiple-dose activated charcoal
    - Hemodialysis
    - Urinary pH alkalization
    - Hyperbaric oxygenation
- **Administration of anti-dotes**
    - Neutralization by antibodies
    - Metabolic antagonism
    - Physiologic antagonism
- **Prevention of re-exposure**
    - Child-proofing
    - Psychiatric referral

N.B-Induction of vomiting is contraindicated in patients who ingested caustic or corrosive substances and hydrocarbons, comatose patients and those with seizures.

INITIAL MANAGEMENT

1. Hypoglycemia

- **40% Dextrose**, IV, 40-60ml over 1-3 minutes

  PLUS

2. Hypotension

- **Normal saline**, IV, 1000ml fast then according to response

3. Seizure management and medicine-associated agitated behavior

- **Diazepam 10mg**, IV, stat repeat doses as needed.
  - o CAUTION-respiratory depression

- **Activated charcoal**, 50gram, P.O., or via NG tube, diluted in 400–800ml water Activated charcoal may reduce systemic absorption of a variety of substances.
  - o The greatest benefit is achieved if activated charcoal is given within one hour after ingestion.
  - o When mixing, add a small amount of water to charcoal in a container cap and shake container to make a slurry and then dilute further.

CATHARSIS

- Should be given only with the first dose of multiple dose charcoal in order to prevent electrolyte abnormalities and osmotic diuresis.
- **Magnesium sulphate**, 250mg/kg

  OR

- **Sodium sulfate**, 250mg/kg

ALKALIZATION OF URINE

- This is a high-risk procedure and should only be performed in consultation with a specialist.
- May be of benefit in salicylate, lithium, barbiturate and, tricyclic antidepressant poisoning.

- **Sodium bicarbonate**, IV, 50–100mEq in 1 L sodium chloride 0.45%. Administer 250–500mL over 1–2 hours. Attempt to achieve urine pH of 7.5.

Table 15. 3. Common antidotes (adapted from hand book for the management of poisoning and overdose, Singapore MOH, 2000)

Poison	Antidote(s)	Dose for adults
Carbon monoxide	Oxygen	high-flow oxygen by tight-fitting facemask or ventilator
Benzodiazepines	Flumazenil	Initial dose: 0.1-0.2mg IV over 30-60 sec, repeat 0.1-0.2mg IV every minute up to 1mg
Acetaminophen	N-acetylcysteine	Initial oral dose: 140mg/kg, then 70mg/kg q 4h x 17 doses
Heparin	Protamine sulfate	1 mg neutralizes 90-115 U heparin; Initial dose: 1 mg/min to total dose 200mg in 2 h
Isoniazid	Pyridoxine (Vitamin B6)	Initial dose: 1 gm pyridoxine for every gm INH ingested or empiric 5gm IV over 10 min if amount ingested unknown

Opiates	Naloxone	Initial dose: 0.1-2.0mg IV push (opioid dependent patients should receive 0.1 mg IV every 30-60 sec until clinical response)
Ticyclic antidepressants	Sodium bicarbonate	Initial dose: 1-2 ampules (50-100mEq) IV push, then IV infusion to maintain blood pH 7.45-7.55 (Preparation: 3 amps 50mEq of NaHCO3 in 1liter D5W infused at 200-250 mL/h)
Organophosphates Carbamates Nerve agents	Atropine	Initial dose: 0.5-2.0mg IV; repeat q 3-5 min until sweat and secretions clear
	Pralidoxime	Initial dose: 1 gm IV over 15 min, then IV infusion of 3-4mg/kg/h for 24-72 hrs

15.10.2 SPECIFIC POISONS AND OVERDOSES

CARBAMATES AND ORGANOPHOSPHATES

BRIEF DESCRIPTION

- Poisoning due to parathion, malathion and other organophosphates.
- Absorption occurs through the skin or the agent is taken orally.
- Patients present with muscarinic and nicotinic manifestations of intoxication.

CLINICAL FEATURES

- The killer signs are the 3B's: bradycardia, bronchospasm and bronchorrhea
- Muscarinic overstimulation causes salivation, lacrimation, vomiting, diarrhea and increased bronchial secretions.
- Nicotinic overstimulation causes muscle fasciculations and paresis or paralysis.
- Patients may present with either bradycardia or tachycardia.

INVESTIGATIONS

- Clinical
- Toxicological analysis

TREATMENT

- For all poisoning patients the principles of management are
    - ABC's of life comes first,
    - Give coma cocktail (Naloxone, thiamine, dextrose and oxygen),
    - decontamination,
    - Antidote and,
    - Supportive care

OBJECTIVES

- Support physiological function
- Treat symptoms
- Remove the poison from the body

NON PHARMACOLOGIC

- Supportive treatment

Pharmacologic

- **Atropine**, IV, 1-3 mg, every 3-5 minutes, until pulmonary secretions are dry
- Do not stop atropine therapy abruptly. Wean the rate of administration slowly.
- During weaning monitor the patient for possible worsening.
- Our goal in atropinazation is chest clearance and not tachycardia.

CARBON MONOXIDE

CLINICAL FEATURES

- Poisoning with carbon monoxide is common where there is incomplete combustion of charcoal.
- Acute poisoning results in headache, nausea and vomiting, mental confusion and agitation.
- Severe toxicity causes confusion, impaired thinking, and may progress to coma, convulsions, and death.

INVESTIGATIONS

- Clinical
- Toxicological analysis

TREATMENT

OBJECTIVES

- Support physiological function
- Treat symptoms
- Remove the poison from the body

Non pharmacologic

- Supportive treatment

- Take the patient out to open air.

PHARMACOLOGIC

- **Oxygen**, 100% via face mask

BARBITURATES (COMMONLY PHENOBARBITONE)

CLINICAL FEATURES

- Overdose is associated with depression of the CNS, coma, hypotension, loss of reflexes, hypothermia, respiratory arrest, and death.
- A characteristic of a barbiturate overdose is the persistence of the pupillary light reflex even with stage IV coma.
- Bullous skin lesions often occur over the hands, buttocks and knees.

INVESTIGATIONS

- Clinical
- Toxicological analysis (determination of barbiturate levels)

TREATMENT

OBJECTIVES

- Support physiological function
- Treat symptoms
- Remove the poison from the body

Non-pharmacologic

- Mechanical ventilation required in severe cases
- Hemodialysis

Pharmacologic

- **Activated charcoal –** see doses above
- Multiple-dose activated charcoal every 4 to 6 hours is specifically indicated

PLUS

- **Alkaline diuresis**-see above

15.11 ENVIRONMENTAL EMERGENCIES

15.11.1 BURN

- Burn is a traumatic injury to the skin or other tissues caused by thermal, chemical, electrical, radiation or cold exposures. Burns are an acute wound and pass-through series of healing steps. The most common type of burn in children is from a scald injury; in adults, the most common burn occurs from a flame.

Table 15. 4. Classification of burns based on the depth of injury (Adapted from, Med Clin North Am 1997 and Am Fam Physician 1992)

Depth	Appearance	Sensation	Healing time
First degree (Superficial)	Dry (no blister) Erythematous Blanches with pressure	Painful	3-6 days
Second degree (partial- thickness)-superficial	Blisters Moist, red, weeping Blanches with pressure	Painful (even to air)	7 to 21 days
Second degree (partial- thickness)-deep	Blisters (easily unroofed) Wet or waxy dry Variable color (cheesy white to red) Does not blanch with pressure	Senses pressure only	Perceptive >21 days-requires surgical treatment
Third degree (full thickness)	Waxy white to gray or black Dry and inelastic No blanching with pressure	Deep pressure only	Rare, unless surgically treated
Fourth degree (extending beyond the skin)	Extends into fascia and/or muscle	Deep pressure only	Never, unless surgically treated

A thorough and accurate estimation of burnt surface area is essential to guide therapy.

Table 15. 5. Burn injury severity grading (modified from the American Burn Association burn injury severity grading system. J Burn Care Rehabil 1990)

Burn type	Criteria	Disposition
Minor	<10% TBSA burn in adults <5%TBSA burn in young or old <2% full-thickness burn No face, hand, perineum or feet involvement	Outpatient
Moderate	10-20%TBSA burn in adults 5-10% TBSA burn in young or old 2-5% full-thickness burn High voltage injury Suspected inhalation injury Circumferential burn Medical problem predisposing to infection (e.g., diabetes mellitus)	Admit
Major	>20% TBSA burn in adults >10% TBSA burn in young or old >5 %full-thickness burn High voltage burn Known inhalation injury Any significant burn to face, eyes, ears, genitalia, or joints Significant associated injuries (fracture or other major trauma)	Refer after emergency management (Make sure the referral center provides burn services)

TBSA: total body surface area; Young or old: <10 or >50 years old; Adults: >10 or <50 years old

TREATMENT

OBJECTIVES

- Prevent ongoing burn
- Secure airway and maintain ventilation
- Correction of fluid and electrolyte deficits
- Prevention and management of infection
- Avoid or minimize permanent disability

Non pharmacologic

Emergency measures

- Remove clothing and jewelry.
- Maintain adequate airway and give oxygen via face mask
- Consider early intubation for any sign of breathing difficulty, airway burn, swelling, or suspected inhalation injury, full-thickness burns of the face or perioral region, circumferential neck burns, acute respiratory distress, progressive hoarseness or air hunger, respiratory depression or altered mental status,
- Establish two large-bore peripheral IV lines in unburned skin.
- Insert NG tube and avoid oral fluids in children with burns greater than 15% BSA and adults with partial thickness burns of >20% of body surface area due to frequent development of ileus.
- Insert Foley catheter
- Wrap all wounds with sterile towels until further decision is made.

PHARMACOLOGIC MANAGEMENT

Fluid resuscitation

- Ringer's lactate or NS 4mL/kg/% BSA burned: 1/2 the fluid is given over the first 8 hrs calculated from the time of onset of the injury and the remaining 1/2 is given at an even rate over the next 16 hrs. (Parkland formula)

- The rate of the infusion is adjusted according to the patient's response to therapy.
- Adequacy of the resuscitation is reflected by vital signs, skin turgor, adequate urine output (1mL/kg/hr. in children and 0.5 mL/kg in adults). Clinical signs of adequate perfusion are monitored every hour for the first twenty-four hours
- During the 2nd 24 hrs. patients begin to reabsorb edema fluid and to diurese. ½ of the first day fluid requirement is needed as Ringer's lactate in 5% dextrose.
- Oral supplementation may be started after 48hr post burn

ESTIMATE BODY SURFACE AREA OF THE BURNT BODY-SEE ANNEX 15

PHARMACOLOGIC MANAGEMENT

WOUND MANAGEMENT

MINOR BURNS

- Treated in an outpatient setting
- Debride all loose skin. Blisters are better not excised
- Cleanse with mild soap and irrigate with isotonic saline.
- The wound is then covered with Silver sulfadiazine and properly dressed.
- The first dressing change and dressing evaluations are performed 24-48 hrs after injury
- **Silver sulfadiazine cream 1%,** apply daily with sterile applicator (not on the face or in patients with a sulfa allergy)

  OR

- **Fusidic acid**, thin films of 2% cream applied to skin 3-4 times daily.

MODERATE AND SEVERE BURNS

- Do all recommended for minor burns

- Apply local antibiotic or Vaseline coated dressing
- Antibiotic prophylaxis is not recommended unless there is obvious infection.

Prevention of stress ulcer – for severe burns only

First line for patients who are able to take oral medications

- **Omeprazole**, 40mg, oral, daily
- **First line** for patients who are unable to take oral medications
- **Cimetidine**, 200mg-400mg IV, every 12 hours

TETANUS PROPHYLAXIS

- **Tetanus immunization** should be updated for any burns deeper than superficial-thickness.

PAIN MANAGEMENT:

First line use depending on pain severity and response in step wise fashion

- **Paracetamol**, 500-1000mg P.O., 4-6 times a day

  OR

- **Tramadol** 50-100mg, Slow IV or P.O, 3-4 times daily (maximum 400mg/day)

  OR

- **Morphine hydrochloride injection** (for severe pain only), 10-20 mg IM OR SC, repeat every 4 hours PRN.

  OR

- **Pethidine** 50mg IM every 4 hrs (depending on the need) or 5-10 mg IV 5 minutes

SYSTEMIC ANTIBIOTICS

- Not indicated for prophylaxis
- When there is evidence of infection (e.g. persistent fever, leukocytosis) take

specimens for culture and start empiric antibiotics based on suspected site of infection.

- If wound infection is the suspected source of infection empiric antibiotics should cover *Pseudomonas aeruginosa*, other gram-negative bacteria's and *Staphylococcus aureus*

PREVENTION, MANAGEMENT AND FOLLOW UP OF COMPLICATIONS

- Electrolytes-Hyperkalemia, hyponatremia/hypernatremia
- Acute Kidney Injury-Correction fluid deficit, avoidance of nephrotoxic medication
- Malnutrition-burn patients require high calorie and high protein diet
- Deep vein thrombosis-Prophylaxis with heparin if patient is immobilized
- Joint Contractures-proper wound care and physiotherapy
- Psychiatric attention
- Urine output should be strictly followed with goal of 1-2ml/kg/hr, do urinalysis to check for rhabdomyolysis
- Always suspect and report burns mainly in children and the elderly as abuse especially hand and glove type of pattern

15.11.2 MAMMALIAN AND HUMAN BITES

BRIEF DESCRIPTION

- Dog bites-cause a range of injuries from minor wounds (scratches, abrasions) to major complicated wounds (deep open lacerations, deep puncture wounds, tissue avulsions).
- Cat bites-scratches typically occur on the upper extremities or face. Deep puncture wounds are of particular concern because cats have long, slender, sharp teeth. When the hand is the target of such a puncture wound, bacteria can be inoculated below the periosteum or into a joint and result in osteomyelitis or septic arthritis.

- Human bites – human bites cause a semicircular or oval area of erythema or bruising that is usually visible; the skin itself may or may not be intact.
- The predominant organisms in animal bite wounds are the oral flora of the biting animal (notable pathogens include Pasteurella, Capnocytophaga, and anaerobes) as well as human skin flora (such as staphylococci and streptococci).

CLINICAL FEATURES

- Pain
- Bleeding
- Swelling
- Teeth impression on bitten site
- Foreign body
- Fever
- Tenderness

INVESTIGATIONS

- CBC
- X-ray of the affected area if bone involvement
- Ultrasound of the abdomen if visceral involvement suspected
- Culture from the wound discharge

TREATMENT

OBJECTIVES

- Treat associated infections
- Prevent tissue loss

Non pharmacologic

Wound care

- The surface should be cleaned with 1% povidone iodine
- Irrigate the depths with copious amounts of saline using pressure irrigation.
- Debridement of devitalized tissue
- Explored to identify injury to underlying structures and presence of a foreign body
- For dog bites: easy mneumonic:
- RATS. Rabies, antibiotics, tetanus and soap

Primary closure

- Nearly all cat, human and most dog bites are left open (to heal by secondary intention).
- When primary closure is strongly considered because of cosmetic reasons the wound should be:
  - Clinically uninfected,
  - Less than 12 hours old
  - NOT located on the hand or foot

PHARMACOLOGIC

Antibiotic prophylaxis Indications

- Deep puncture wounds
- Associated crush injury
- Wounds on the hand (s) or in close proximity to a bone or joint
- Wounds requiring closure
- Bite near or in a prosthetic joint
- Cat bites
- Delayed presentation > 12 hours for most wounds
- Bite wounds in compromised hosts (e.g., immunocompromised and adults with diabetes mellitus)

First line

- **Amoxycillin-clavulanate**, 500/125mg, P.O., TID for 3-5 days or 875/125 mg, P.O., BID for 3-5 days

Alternative

- **Doxycycline**, 100mg, P.O., BID for 3-5 days

  OR

- **Cotrimoxazole** 960mg, P.O., BID for 3-5 days

  OR

- **Cefuroxime** 500mg, P.O., BID for 3-5 days

  PLUS

- **Metronidazole** 500mg, P.O., TID for 3-5 days

NB: Cloxacillin and cephalexin should be avoided in human, dog or cat bites

1. INFECTION TREATMENT

- For infected wound use the above antibiotics mentioned for prevention but for prolonged duration 10-14 days

2. TETANUS AND RABIES PREVENTION

- **Tetanus toxoid (TT)**, I.M.0.5ml once, for primary or booster immunization
- **TAT** (Tetanus Antitoxin), 3000 units, SC, stat, for all adults with animal or human bites except for those with clean and minor wounds after skin test
- **Rabies prophylaxis** both passive administration of rabies immune globulin (with as much of the dose as possible infiltrated into and around the wound) and active immunization
- For the details see the "Rabies" section, under the infectious disease chapter.

15.11.3 SNAKE BITES

BRIEF DESCRIPTION

- The majority of snakebites are non–poisonous; only few species are venomous (poisonous).
- Most common venomous snakes are the pit vipers (vasculotoxic) and the elapidae and hydrphidae (primarily neurotoxic).
- Children, because of their smaller body size, are far more likely to have severe envenomation.

CLINICAL FEATURES

- Cranial nerve paralysis-ptosis, ophthalmoplegia, slurred speech
- Bulbar respiratory paralysis-drooling, and inability to breath properly
- Impaired consciousness, seizures
- Meningism
- Tender and stiff muscles
- Rapid progression of swelling to more than half of bitten limb
- Blistering, necrosis and bruising
- Fascial compartmentalization on bitten digits.
- oral swelling or paresthesia's, metallic or rubbery taste in the mouth, hypotension,
- tachycardia.
- Anaphylaxis reaction could occur

INVESTIGATIONS

- CBC
- BUN and Creatinine, electrolytes
- 20 minutes whole blood clotting test (leave 2-5ml of blood in dried test tube. Failure to clot after 20 minutes implies incoagulable blood)

- Liver function test

N.B. Avoid venopuncture in state of generalized bleeding

TREATMENT

OBJECTIVES

- Relieve pain and anxiety
- Support the respiration or circulation if indicated
- Counteract the spread and effect of the snake venom
- Prevent secondary infection

Non pharmacologic

First Aid

- Move patient to a safe area
- Remove anything tight around the bitten area (ankle bracelets, Rings)
- Immobilization/splinting of the affected limb.
- Do not move the limb
- Carry the person on a stretcher and tie the limb to a straight piece of wood.
    - C lean the wound and reassure the patient.

At the hospital

- Bed rest, reassure, keep warm
- Assess patient's airway, breathing and circulation (ABC of resuscitation)
- For probable venomous bites:
    - Clean site of bite with antiseptic lotion or soap and water
    - Do not attempt to suck or make any incisions at the site of the bite
    - Leave wound open; punctured wounds are especially likely to be infected.

  - If the snake is identified as non-poisonous or there is absence of swelling or systemic signs after 6 hours reassure the patient
  - Surgical debridement when required

PHARMACOLOGIC

Secondary infection:

First line

- **Amoxicillin/clavulanic acid,** oral, 500/125mg, TID for 5-7 days.
- **Immunization, primary or booster**:
- **Tetanus toxoid vaccine**, IM, 0.5mL immediately.

Analgesia

For mild pain:

- **Paracetamol**, 1 g 4–6 P.O., hourly when required to a maximum of 4 doses per 24 hours.

For severe pain:

ADD

- **Tramadol**, 50-100mg, 2-3X per day

N.B. The use of an NSAID is not recommended due to the potential danger of Acute Kidney Injury in a hypotensive patient.

POLYVALENT ANTIVENOM

Indications for polyvalent antivenom:

- worsening of local injury (e.g., pain, ecchymosis, or swelling), abnormal results on laboratory tests (e.g., worsening platelet count, prolonged coagulation times), or systemic manifestations (e.g., unstable vital signs or abnormal mental status).
- All patients with confirmed mamba bites before symptom onset
- Patients with confirmed puff adder or Gaboon adder bites should receive antivenom at the onset of any symptoms

N.B.

- In most cases patients do not need and should not be given antivenom.
- The dose of antivenom is the same for adults and children.
- Serum sickness is a relatively common adverse event.
- Even after the administration of antivenom, patients with neurotoxic snakebites may need ventilation.

POLYVALENT SNAKE ANTIVENOM, SLOW IV INFUSION. DILUTE 100 ML IN 300ML OF NS.

- Have resuscitation tray ready (adrenaline 1: 1000)
- Test dose-0.2 ml, subcutaneous, to test for anaphylaxis
- Administer slowly for the first 15 minutes, as most allergic reactions will occur within this period.
- Increase the flow rate gradually to complete the infusion within one hour.
- Continue to observe for progression of edema and systemic signs of envenomation during and after antivenom infusion. Measure limb circumference at several sites above and below the bite, and outline the advancing border of edema with a pen every 30 minutes. These measures serve as an index of the progression as well as a guide for antivenom administration.
- Repeat laboratory determinations every 4 hours or after each course of antivenom therapy, whichever is more frequent. Repeat if there is no clinical improvement after the infusion.
- Mild hypersensitivity reactions should not be a reason not to give polyvalent.
- If there are signs of compartment syndrome elevate the leg, consider additional dosing of the infusion and consider fasciotomy if there is no response for conservative management.

15.11.4 NEAR DROWNING

BRIEF DESCRIPTION

- Drowning is death from suffocation (asphyxia) following submersion in a liquid medium.
- Near-drowning is survival, at least temporarily, after suffocation with/without loss of consciousness.

RISK FACTORS OF NEAR-DROWNING:

- Inability to swim or overestimation of swimming capabilities.
- Risk-taking behavior.
- Use of alcohol and/or illicit medicines.
- Inadequate adult supervision.
- Hypothermia, which can lead to rapid exhaustion or cardiac arrhythmias.
- Concomitant trauma, cerebrovascular accident, or myocardial infarction.
- Undetected primary cardiac arrhythmia,
- Hyperventilation prior to a shallow dive which can lead to cerebral hypoxia, seizures, and loss of consciousness, which again can result in drowning.

CLINICAL FEATURES

- Shortness of breath, difficulty breathing, apnea
- Persistent cough, wheezing
- In stream, lake, or salt water immersion, possible aspiration of foreign material
- Level of consciousness at presentation, history of loss of consciousness, anxiety
- Vomiting, diarrhea
- Bradycardia or tachycardia, dysrhythmia
- Clinical deterioration mostly develops within 7 hours of immersion.

- Suffocation by submersion leads to hypoxemia by means of either aspiration or reflex laryngospasm. Hypoxemia in turn affects every organ system, with the major being cerebral hypoxia.

TREATMENT

OBJECTIVES

- Quickly restoring ventilation and oxygenation
- Prevent end organ damage Has three phases: prehospital care, emergency unit care, and inpatient care.

PREHOSPITAL CARE

- Rapid cautious rescue Cervical spine precautions
- Cardiopulmonary resuscitation (CPR) as indicated, oxygen for all patients and transport
    - CPR should be done as soon as possible without compromising the safety of the rescuer or delaying the removal of the victim from the water.
- High flow supplemental oxygen should be administered to the spontaneously breathing patient by facemask, while the apneic patient should be intubated.
- Rewarming all hypothermic patients with a core temperature <33°C should be initiated, either by passive or active means as available.

N.B. The Heimlich maneuver or other postural drainage techniques to remove water from the lungs have no proven value.

EMERGENCY UNIT MANAGEMENT

- **Rule out** injuries to the axial skeleton and internal injuries to the abdomen and chest.
- **Elective intubation:** In the symptomatic patient, indications for elective intubation include signs of neurologic deterioration and an inability to maintain a SPO2 >90mmHg on high fractions of supplemental oxygen.

INPATIENT MANAGEMENT

- Symptomatic patients require hospitalization for supportive care and treatment of organ specific complications.

USEFUL MODALITIES OF TREATMENT:

- Mild hyperventilation to reduce intracranial pressure.
- Elevate head of the bed, if potential cervical spine injuries are excluded.
- Diuretics to avoid hypervolemia
- Seizure activity should be controlled. Phenytoin is the preferred agent as it does not depress consciousness.
- Manage both hypoglycemia and hyperglycemia

RESPIRATORY FAILURE

- Bronchospasm is treated similarly to acute asthma; most cases rapidly improve with inhaled beta-adrenergic agonists.
- Antibiotics should be used only in cases of clinical pulmonary infection or if the victim was submerged in grossly contaminated water.

HYPOTENSION

- Persons with hypothermia can have significant hypovolemia and hypotension due to a “cold diuresis.” Optimal fluid replacement and inotropic support.
- If Glasgow coma scale (GCS)>13, PSO2 >96%, and clear concomitant traumas, monitor O2, and observe for 4-6 hours,
    - reassess patient chest condition, mentation, and PSO2, and
    - if normal discharge home
- If GCS<13, PSO2 <96 keep patient for rigorous care, and
    - if need for intubation or non-invasive ventilation (NIV) refer to a center with ICU.

CHAPTER 16:

PEDIATRIC DISORDERS

16.1 PEDIATRIC EMERGENCIES

16.1.1 TRIAGE

- **Triage** is the process of rapidly screening sick children soon after their arrival in hospital, in order to identify:
    - Those with **emergency signs**, who require immediate emergency treatment;
    - Those with **priority signs**, who should be given priority in the queue so that they can be assessed and treated without delay; and
    - Non-urgent cases, who have neither emergency nor priority signs.
- **Emergency signs** include:
    - Obstructed or absent breathing
    - Severe respiratory distress
    - Central cyanosis
    - Signs of shock (cold hands, capillary refill time longer than 3 s, high heart rate with weak pulse, and low or immeasurable blood pressure)
    - Coma (or seriously reduced level of consciousness)
    - Convulsions
    - Signs of severe dehydration in a child with diarrhea (lethargy, sunken eyes, very slow return after pinching the skin or any two of these).
- Children with these signs require **immediate** emergency treatment to avert death.

- The **priority signs**
  - identify children who are at higher risk of dying.
  - These children should be **assessed without unnecessary delay**.
  - If a child has one or more emergency signs, don't spend time looking for priority signs.
- Steps in emergency triage assessment and treatment are summarized as
- **First check for emergency signs** in three steps:
  - **Step 1.** Check whether there is any airway or breathing problem; start immediate treatment to restore breathing. Manage the airway and give oxygen.
  - **Step 2.** Quickly check whether the child is in shock or has diarrhea with severe dehydration. Give oxygen and start IV fluid resuscitation. In trauma, if there is external bleeding, compress the wound to stop further blood loss.
  - **Step 3.** Quickly determine whether the child is unconscious or convulsing. Give IV glucose for hypoglycaemia and/or an anti-convulsant for convulsing.
- **If emergency signs are found:**
  - Call for help from an experienced health professional if available, but do not delay starting treatment.
  - Stay calm and work with other health workers who may be required to give the treatment, because a very sick child may need several treatments at once.
  - The most experienced health professional should continue assessing the child to identify all underlying problems and prepare a treatment plan.
  - Carry out emergency investigations (blood glucose, blood smear, hemoglobin [Hb]).
  - Send blood for typing and cross matching if the child is in shock, appears

to be severely anaemic or is bleeding significantly.

  - After giving emergency treatment, proceed immediately to assessing, diagnosing and treating the underlying problem.

- **If no emergency signs are found, check for priority signs:**
  - **T**iny infant: any sick child aged < 2 months
  - **T**emperature: child is very hot
  - **T**rauma or other urgent surgical condition
  - **P**allor (severe)
  - **P**oisoning (history of)
  - **P**ain (severe)
  - **R**espiratory distress
  - **R**estless, continuously irritable or lethargic
  - **R**eferral (urgent)
  - **M**alnutrition: visible severe wasting
  - **O**edema of both feet
  - **B**urns (major)
- The above can be remembered from the mnemonic **3TPR MOB**.
- These children need prompt assessment (no waiting in the queue) to determine what further treatment is needed. Move a child with any priority sign to the front of the queue to be assessed next.

FURTHER READING

- Khalili A, Shadi D, Kalvandi N, Nasiri M, Sadegh R. Triage methods in children, a systematic review. Electron J Gen medicine. 2018 Jan 1;15(3).
- Rajasagaram U, Taylor DM, Braitberg G, Pearsell JP, Capp BA. Paediatric pain assessment: differences between triage nurse, child and parent. Journal of paediatrics and child health. 2009 Apr;45(4):199-203.

16.1.2 RESUSCITATION OF THE CHILD

- Total daily maintenance fluid requirement is 100 ml/kg for the first 10 kg plus 50 ml/kg for the next 10 kg plus 25 ml/kg for each subsequent kg
- Give more than above if child is dehydrated or in fluid loss or fever (10% more for each 1°C of fever)
- Monitor IV fluids very carefully because of risk of overload

FLUIDS, WHICH CAN BE USED FOR MAINTENANCE:

- Half normal saline plus 5% or 10% dextrose
- Ringer's lactate with 5% dextrose
- Normal saline with 5% dextrose
- Do not use Dextrose 5% alone
- Monitor IV fluids very carefully because of risk of overload

FLUID MANAGEMENT IN NEONATES

- Encourage mother to breastfeed or if child unable, give expressed breast milk via NGT
- Withhold oral feeding in case of bowel obstruction, necrotizing enterocolitis, or if feeding is not tolerated (abdominal distension, vomiting everything)
- Withhold oral feeding in acute phase of severe sickness, in infants who are lethargic, unconscious or having frequent convulsions

TOTAL AMOUNT OF FLUIDS (ORAL AND/OR IV)

- Day 1: 60 ml/kg/day of Dextrose 10%
- Day 2: 90 ml/kg/day of Dextrose 10%
- Day 3: 120 ml/kg/day of half normal saline and dextrose 5%
- Day 4 onwards: 150 ml/kg/day

PRECAUTIONS AND DIRECTIONS OF FLUID ADMINISTRATION

- If only IV fluids are given, do not exceed 100ml/ kg/day unless child is dehydrated, under a radiant heater or phototherapy
- If facial swelling develops, reduce rate of infusion
- When oral feeding is well established, raise the total amount to 180 ml/ kg/day
- Use Ringer's lactate or normal saline
- Infuse 20 ml/kg as rapidly as possible
- If no improvement: Repeat 10-20 ml/kg of IV fluids
- If bleeding, give blood at 20 ml/kg
- If still no improvement: Give another 20 ml/kg of IV fluids
- If no improvement further still: Suspect septic shock
- Repeat 20 ml/kg IV fluids and consider adrenaline or dopamine
- If improvement noted at any stage (reducing heart rate, increase in blood pressure and pulse volume, capillary refill <2 seconds): Give 70 ml/kg of Ringer's lactate (or Normal saline if Ringer's not available) over 5 hours (if infant <12 months) or 2.5 hours (if child >12 months)

Note

- In children with suspected malaria or anemia with shock, IV fluids should be administered cautiously and blood should be used in severe anemia.

FURTHER READING

1. Kiguli S, Akech SO, Mtove G, Opoka RO, Engoru C, Olupot-Olupot P, Nyeko R, Evans J, Crawley J, Prevatt N, Reyburn H. WHO guidelines on fluid resuscitation in children: missing the FEAST data. Bmj. 2014 Jan 14;348:7003.
2. https://www.uptodate.com/contents/maintenance-intravenous-fluid-therapy-in-children

16.1.3 ANAPHYLAXIS

BRIEF DESCRIPTION

- Severe allergic reaction that occurs rapidly (seconds or minutes) after administration, or exposure, and may be life threatening. It generally affects the whole body.

CAUSES

- Allergy to pollens, some medicines (e.g., penicillin, vaccines, acetylsalicylic acid), or certain foods (e.g., eggs, fish, cow's milk, nuts, some food additives)
- Reaction to insect bites, e.g., wasps and bees

CLINICAL FEATURES

- Body itching, hives (urticarial rash), swelling of lips, eyes, tongue
- Difficulty in breathing (stridor, wheezing)
- Hypotension and sudden collapse, excessive sweating, thin pulse
- Abdominal cramps, vomiting and diarrhea

DIFFERENTIAL DIAGNOSIS

- Other causes of shock, e.g., hemorrhagic (due to bleeding), hypovolemic (severe dehydration), septic
- Asthma, foreign body in airways

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Determine and remove the cause
- Secure the airways

- Restore BP: lay the patient flat and raise feet
- Keep patient warm

PHARMACOLOGIC

- Sodium chloride 0.9% infusion 20 ml/kg by IV infusion over 60 minutes Start rapidly then adjust rate according to BP
- Administer oxygen
- Adrenaline (epinephrine) injection 1 in 1000 (1 mg/ml) Child <6 years: 150 micrograms (0.15 ml), Child 6-12 years: 300 micrograms (0.3 ml) IM immediately, into anterolateral thigh. Repeat every 5-10 minutes according to BP, pulse rate, and respiratory function until better
- In severely affected patients: Hydrocortisone Child <1 year: 25 mg, Child 1-5 years: 50 mg, Child 6-12 years: 100 mg IM or slow IV stat
- If urticaria/itching: Give an antihistamine as useful adjunctive treatment e.g. chlorpheniramine: Child 1-2 years: 1mg every 12 hours, Child 2-5 years: 1 mg every 6 hours, Child 5-12 years: 2 mg every 6 hours
- Promethazine: Child 1-5 years: 5 mg by deep IM, Child 5-10 years: 6.25-12.5 mg by deep IM, Repeat dose every 8 hours for 24-48 hours to prevent relapse, Repeat adrenaline and hydrocortisone every 2-6 hours prn depending on the patient's progress

Notes

- Adrenaline: IM is the route of choice: absorption is rapid and more reliable than SC
- Monitor the patient for several hours (reaction may recur after several hours)
- If drug reaction, compile adverse drug reaction reporting form (see appendix 2)

Prevention

- Always ask about allergies before giving patients new medicine

- Keep emergency drugs at hand at health facilities and in situations where risk of anaphlaxis is high, e.g. visiting bee hives or places that usually harbour snakes
- Counsel allergic patients to wear alert bracelet or tag

FURTHER READING

1. Cheng A, Canadian Paediatric Society, Acute Care Committee. Emergency treatment of anaphylaxis in infants and children. Paediatrics & Child Health. 2011 Jan 1;16(1):35-40.
2. Gonzalez-Estrada A, Silvers SK, Klein A, Zell K, Wang XF, Lang DM. Epidemiology of anaphylaxis at a tertiary care center: a report of 730 cases. Annals of Allergy, Asthma & Immunology. 2017 Jan 1;118(1):80-5.

16.1.4 BURN

BRIEF DESCRIPTION

- Burn is a traumatic injury to the skin or other tissues caused by thermal, chemical, electrical, radiation or cold exposures.
- Burns are acute wound and pass-through series of healing steps.
- The most common type of burn in children is from a scald injury; in adults, the most common burn occurs from a flame.

Table 16. 1. Classification of burns based on the depth of injury (Adapted from, Med Clin North Am 1997 and Am Fam Physician 1992)

Depth	Appearance	Sensation	Healing time
First degree (Super ficial)	Dry (no blister) Erythematous Blanches with pressure	Painful	3-6 days

Second degree (partial-thickness)- superficial	Blisters Moist, red, weeping Blanches with pressure	Painful (even to air)	7 to 21 days
Second degree (partial-thickness)- deep	Blisters (easily unroofed) Wet or waxy dry Variable color (cheesy white to red) Does not blanch with pressure	Senses pressure only	Perceptive >21 days - requires surgical treatment
Third degree (full thickness)	Waxy white to gray or black Dry and inelastic No blanching with pressure	Deep pressure only	Rare, unless surgically treated
Fourth degree (extending beyond the skin)	Extends into fascia and/or muscle	Deep pressure only	Never, unless surgically treated

- A thorough and accurate estimation of burnt surface area is essential to guide therapy.

Table 16. 2. Burn injury severity grading (modified from the American Burn Association burn injury severity grading system. J Burn Care Rehabil 1990)

Burn type	Criteria	Disposition
Minor	<10% TBSA burn in adults <5%TBSA burn in young or old <2 % full-thickness burn	Outpatient
Moderate	10 - 20%TBSA burn in adults 5 - 10% TBSA burn in young or old 2 - 5 % full-thickness burn High voltage injury Suspected inhalation injury Circumferential burn Medical problem predisposing to infection (eg, diabetes mellitus)	Admit
Major	>20% TBSA burn in adults >10% TBSA burn in young or old Any degree of full-thickness burn High voltage burn Known inhalation injury Any significant burn to face, eyes, ears, genitalia, or joints Significant associated injuries (fracture or other major trauma)	Refer after emergency management

TBSA: total body surface area;Young or old: <10 or >50 years old;Adults: >10 or <50 years old

TREATMENT

Objectives

- Prevent ongoing burn
- Secure airway and maitain ventilation
- Correction of fluid and electrolyte deficits
- Prevetion and managemnt of infection
- Avoid or minimize permanent disablity

Non pharmacologic

i) Emergency measures

- Remove clothing and jewelry.
- Maitain adequate airway and give oxygen via face mask.
- Establish an IV line Insert NG tube and avoid oral fluids in children with burns greater than 15% BSA.
- Insert Foley catheter
- Wrap all wounds with sterile towels unti further decision is made.

ii) Fluid resuscitation

- Ringer's lactate or NS 4mL/kg/% BSA burned: ½ the fluid is given over the first 8 hrs calculated from the time of onset of the injury and the remaining ½ is given at an even rate over the next 16 hrs
- The rate of the infusion is adjusted according to the patient's response to therapy.
- Adequacy of the resuscitation is reflected by vital signs, skin turgor, adequate urine output (1mL/kg/hr in children and 0.5 mL/kg in adults). Clinical signs of adequate perfusion are monitored every hour for the first twenty-four hours
- During the 2nd 24 hr patients begin to reabsorb edema fluid and to diurese. ½ of the first day fluid requirement is needed as Ringer's lactate in 5% dextrose.
- Oral supplementation may be started after 48hr post burn

Estimate body surface area of the burnt body

Pharmacologic management

Wound management

A. MINOR BURNS

- Treated in an outpatient setting
- Debride all loose skin. Blisters are better not excised.
- Cleanse with mild soap and irrigate with isotonic saline.
- The wound is then covered with **Silver sulfadiazine** and properly dressed.
- The first dressing change and dressing evaluations are performed 24-48 hrs after injury
    - ○ **Silver sulfadiazine cream 1%,** apply daily with sterile applicator OR
- **Fusidic acid**, thin films of 2% cream applied to skin 3-4 times daily

B. MODERATE AND SEVERE BURNS - REFER

iii) **Tetanus prophylaxis**

Tetanus immunization should be updated for any burns deeper than superficial-thickness..

iv) **Pain Management:**

First Line- use depending on pain severity and response in step wise fashion

Paracetamol, 10mg/kg P.O. 4-6hours, Max 4 doses per day

Ibuprofen for a child > 3months: 5-10mg/kg every 6-8hours, Max 40mg/kg/day

Morphine: infant < 6months: 0.02mg/kg PO every 4hours, >6months: 0.15-0.3mg/kg/dose

SYSTEMIC ANTIBIOTICS

- Not indicated for prophylaxis
- When there is evidence of infection (e.g. persitent fever, leukocytosis) take specimens for culture and start emperic antibiotics based on suspected

site of infection.

- If wound infection is the suspected source of infection emperic antibiotics should cover *Pseudomonas aeruginosa*, other gram negative bacterias and *Staphylococcus aureus*

FURTHER READING

1. Wiseman J, Ware RS, Simons M, McPhail S, Kimble R, Dotta A, Tyack Z. Effectiveness of topical silicone gel and pressure garment therapy for burn scar prevention and management in children: a randomized controlled trial. Clinical rehabilitation. 2020 Jan;34(1):120-31.
2. Nelson 21st ed. National guideline 2016

16.1.5 CARDIAC ARREST

BRIEF DESCRIPTION

- Sudden cardiac arrest (SCA)) refer to the sudden cessation of cardiac activity with hemodynamic collapse, typically due to sustained ventricular tachycardia/ventricular fibrillation when the event is reversed with intervention or spontaneously; if it is not reversed it will be labeled as sudden cardiac death.
- It usually occurs in individuals with structural heart disease but in the absence of detectable clinical findings.
- Acute myocardial ischemia, electrolyte abnormalities, antiarrhythmic drugs and worsening heart failure can precipitate sudden cardiac arrest.

CLINICAL FEATURES

- Instantaneous or abrupt onset collapse with or without prodrome
- Absent pulse, absent or gasping type of breathing, unresponsive

INVESTIGATIONS

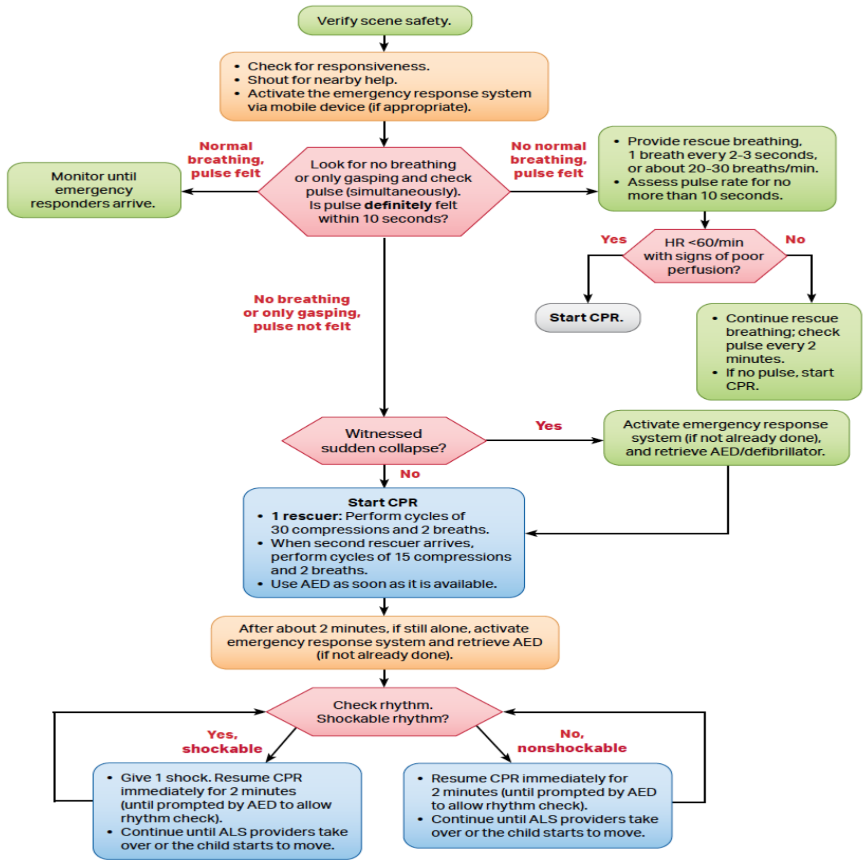
- During the episode no work up is needed except having continuous ECG monitoring together with emergency management.
- Post SCA work up is needed- Troponin, Echocardiography, Electrolytes, RFT

TREATMENT OBJECTIVES

- Achieve adequate ventilation
- Control cardiac arrhythmias
- Stabilize blood pressure and cardiac output
- Restore organ perfusion

Non-pharmacologic

- Provide Basic life support (BLS) and refer with escort


Pediatric Basic Life Support Algorithm for Healthcare Providers—Single Rescuer

Verify scene safety.
• Check for responsiveness. • Shout for nearby help. • Activate the emergency response system via mobile device (if appropriate).
Normal breathing, pulse felt
Monitor until emergency responders arrive.
Look for no breathing or only gasping and check pulse (simultaneously). Is pulse definitely felt within 10 seconds?
No normal breathing, pulse felt
• Provide rescue breathing, 1 breath every 2-3 seconds, or about 20-30 breaths/min. • Assess pulse rate for no more than 10 seconds.
Yes
HR <60/min with signs of poor perfusion?
No
Start CPR.
• Continue rescue breathing; check pulse every 2 minutes. • If no pulse, start CPR.
No breathing or only gasping, pulse not felt
Witnessed sudden collapse?
Yes
Activate emergency response system (if not already done), and retrieve AED/defibrillator.
No
Start CPR
• 1 rescuer: Perform cycles of 30 compressions and 2 breaths. • When second rescuer arrives, perform cycles of 15 compressions and 2 breaths. • Use AED as soon as it is available.
After about 2 minutes, if still alone, activate emergency response system and retrieve AED (if not already done).
Check rhythm. Shockable rhythm?
Yes, shockable
No, nonshockable
• Give 1 shock. Resume CPR immediately for 2 minutes (until prompted by AED to allow rhythm check). • Continue until ALS providers take over or the child starts to move.
• Resume CPR immediately for 2 minutes (until prompted by AED to allow rhythm check). • Continue until ALS providers take over or the child starts to move.

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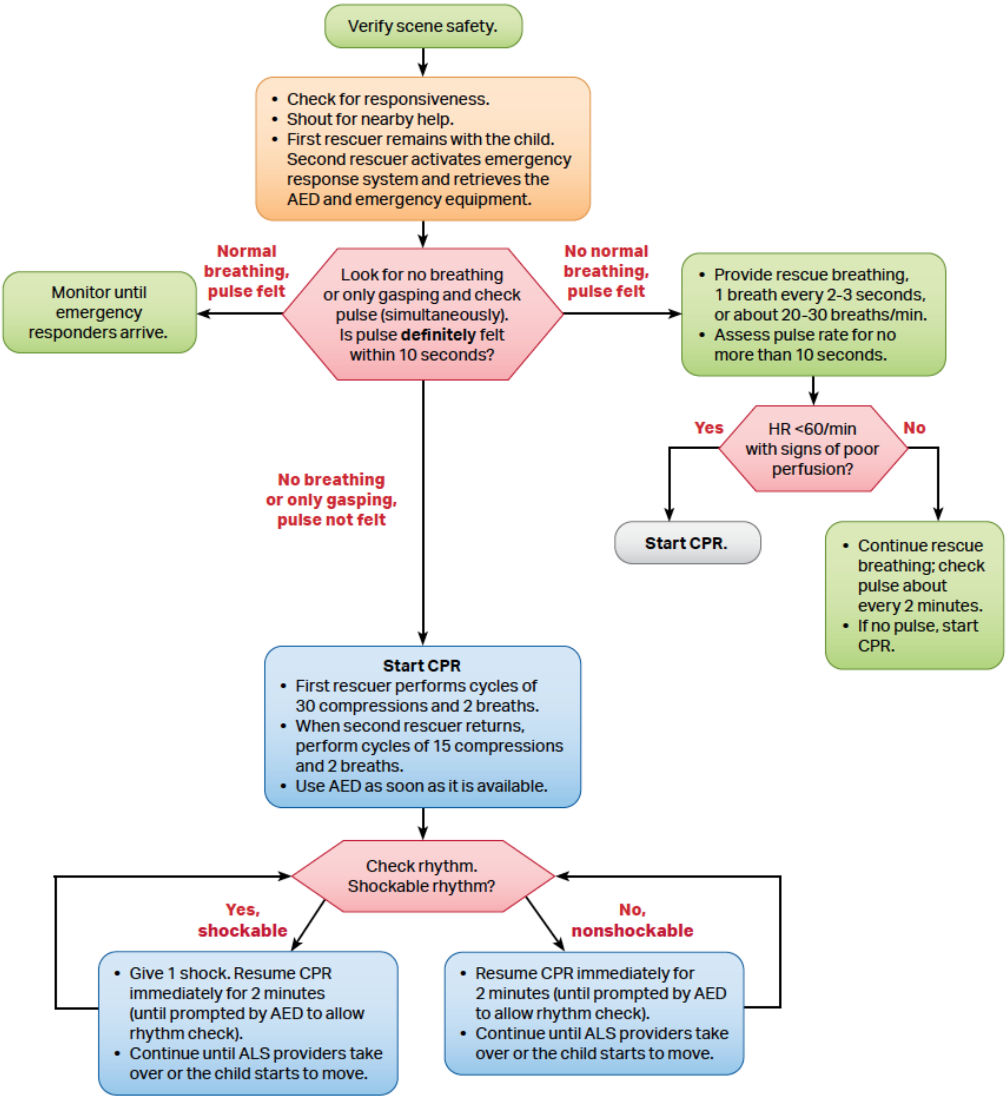
Fig 16.1: BLS guideline (adapted from the 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care)

Pediatric Basic Life Support Algorithm for Healthcare Providers—2 or More Rescuers


Verify scene safety.
• Check for responsiveness.
• Shout for nearby help.
• First rescuer remains with the child. Second rescuer activates emergency response system and retrieves the AED and emergency equipment.
Normal breathing, pulse felt
Monitor until emergency responders arrive.
Look for no breathing or only gasping and check pulse (simultaneously). Is pulse **definitely** felt within 10 seconds?
No normal breathing, pulse felt
• Provide rescue breathing, 1 breath every 2-3 seconds, or about 20-30 breaths/min.
• Assess pulse rate for no more than 10 seconds.
HR <60/min with signs of poor perfusion?
Yes
Start CPR.
No
• Continue rescue breathing; check pulse about every 2 minutes.
• If no pulse, start CPR.
No breathing or only gasping, pulse not felt
Start CPR
• First rescuer performs cycles of 30 compressions and 2 breaths.
• When second rescuer returns, perform cycles of 15 compressions and 2 breaths.
• Use AED as soon as it is available.
Check rhythm. Shockable rhythm?
Yes, shockable
• Give 1 shock. Resume CPR immediately for 2 minutes (until prompted by AED to allow rhythm check).
• Continue until ALS providers take over or the child starts to move.
No, nonshockable
• Resume CPR immediately for 2 minutes (until prompted by AED to allow rhythm check).
• Continue until ALS providers take over or the child starts to move.

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16.1.6 FOREIGN BODY ASPIRATION

BRIEF DESCRIPTION

- Foreign body aspiration is a common problem in children aged 6 months to 4 years.
- Commonly aspirated materials include: nuts, seeds, or other small objects.
- The foreign body commonly lodges in the bronchus, usually the right one.
- The obstruction can lead to collapse or consolidation of portion of the lung distal to the site of obstruction.

CLINICAL FEATURES

- Choking at the time of aspiration followed by symptom free interval
- Chronic cough
- Persistent wheeze, usually unilateral
- Localized area of decreased air entry which is either dull or hyper resonant
- Deviation of trachea and/or apex beat to one side of the chest
- Symptoms/signs of pneumonia, which fail to respond to antibiotic treatment
- If a large foreign body is aspirated, it may lodge in the trachea and may lead to asphyxia and sudden death.

INVESTIGATIONS

- Diagnosis of foreign body aspiration is generally clinical based on a classic history of choking episode or high index of suspicion.
- Chest X-ray may show aspirated material if it is radio-opaque or may show unilateral or localized collapse or hyperinflation of the lung or mediastinal shift
- Bronchoscopy will help for accurate diagnosis as well as removal of the foreign body.

TREATMENT

Non-pharmacologic

- Attempt to dislodge and expel the foreign body as an emergency first aid for the choking child.

For infants:

- Lay the infant on one arm or on the thigh in a head down position.
- Strike the infant's back five times with the heel of the hand.
- If the obstruction persists, turn the infant over and give five chest thrusts with two fingers, one finger's breadth below the nipple level in the midline.
- If the obstruction persists, check the infant's mouth for any obstruction, which can be removed.
- If necessary, repeat this sequence with back slaps again.

For older children:

- While the child is sitting, kneeling or lying, strike the child's back five times with the heel of the hand.
- If the obstruction persists, go behind the child and pass your arms around the child's body; form a fist with one hand immediately below the sternum; place the other hand over the fist and thrust sharply upwards in to the abdomen (Heimlich's maneuver). Repeat this up to five times.
- If the obstruction persists, check the child's mouth for any obstruction which can be removed.
- If necessary, repeat the sequence with backslaps again.
    - o Once this has been done, it is important to check the patency of the airway by:
        - A. Looking for chest movements.
        - B. Listening for air entry, and
        - C. Feeling for breath.

- If the above measures are unsuccessful,
    - Refer the child to a center that can make correct diagnosis and remove the foreign body through bronchoscopy.

Pharmacologic

- If there is evidence for pneumonia start antibiotics (see section on treatment of pneumonia)

FURTHER READING

1. Naqvi S, Siddiqi R, Hussain SA, Batool H, Arshad H. School children training for basic life support. J Coll Physicians Surg Pak. 2011 Oct 1;21(10):611-5.
2. Ralston ME, Day LT, Slusher TM, Musa NL, Doss HS. Global pediatric advanced life support: improving child survival in limited-resource settings. The Lancet. 2013 Jan 19;381(9862):256-65.

16.1.7 SHOCK

BRIEF DESCRIPTION

- Shock is a state of circulatory collapse leading to reduction in delivery of oxygen and other nutrients to vital organs which if prolonged leads to irreversible multiple organ failure.

CAUSES

- Hypovolemic
- Cardiogenic
- Septic shock
- Hypoadrenal
- Anaphylactic

CLINICAL FEATURES

- Palpitations/fatigue/dizziness/fainting, sweating

- Restlessness, clouding of consciousness, cold extremities
- Tachycardia, systolic BP < 90 mmHg

TREATMENT

OBJECTIVES

- Reverse shock
- Maintain airway, breathing and circulation
- Prevent complications
- Prevent death

Non-pharmacologic

- Raise foot end of bed
- Pericardiocentesis for cardiac tamponade

Pharmacologic

16.1.7.1CARDIOGENIC SHOCK (PUMP FAILURE)

First line

- **Norepinephrine (Noradrenaline)**, Initial: 0.5-1 mcg/minute and titrate to desired response; 8-30 mcg/minute is usual range OR
- **Dobutamine**., 2.5-20 micrograms/kg/min IV diluted in dextrose 5%.

Alternatives

- **Dopamine**, 5-20mcg/kg/min IV diluted with dextrose 5% in Water, or in sodium chloride solution 0.9% OR
- **Adrenaline,** I.V. infusion: Initial: 0.1-0.5 mcg/kg/minute (7-35 mcg/minute in a 70 kg patient); titrate to desired response

16.1.7.2 HYPOVOLEMIC SHOCK

- **Infusion of fluid (Normal Saline or Ringer lactate)** 1-2 liters fast; reassess the patient for adequacy of treatment; if needed repeat the bolus with maximum tolerated dose being 60 – 80 ml/kg with in the first 1 – 2 hr.

- For non-malnourished 20ml/kg fast, can be repeated if no response up to 3 times
- For malnourished children 15ml/kg over 1 hour, can be repeated if patient has improvement but still hypovolemic. Consider septic shock if patient deteriorates or not improved after the first bolus
- If due to hemorrhage, transfusion of packed Red Blood Cells (RBC) or whole blood 20ml/kg over 4 hrs. , repeated as needed until Hgb level reaches 10gm/dl and the vital signs are corrected.

16.1.7.3 SEPTIC SHOCK.

- Adequate organ system perfusion with IV fluids (Large volume of IV fluids are required in septic shock patients)

First line

- **Adrenaline,** I.V. infusion: Initial: 0.1-0.5 mcg/kg/minute (7-35 mcg/minute in a70 kg patient); titrate to desired response

Alternatives

- **Dopamine,** 5-50 mcg/kg/min IV diluted with dextrose 5% in Water, or in sodium chloride solution 0.9%; **OR**
- **Norepinephrine (Noradrenaline),** Initial: 0.5-1 mcg/minute and titrate to desired response; 8-30 mcg/minute is usual range **OR**
- **Dobutamine,** 2.5-40 micrograms/kg/min IV diluted in dextrose 5% PLUS
- **Hydrocortisone,** 50 mg/m ^{2} /day IV every 6 hrs (when vasopressor dependent)

16.1.7.4 ADRENAL CRISIS

- Normal Saline Large volumes (1 to 3 liters) or 5 % dextrose in 0.9% percent saline should be infused intravenously / infusion like hypovolemic shock.

  - **Hydrocortisone**, 200mg, IV, stat then 100mg, IV, QID

Supplemental therapies

- Blood transfusion considered for Hgb < 10 g/dL (ideal threshold for transfusion unknown)
- Sedation/analgesia while ventilated
- Optimize oxygenation through ventilation

THERAPEUTIC ENDPOINTS

Clinical

- Heart Rate normalized for age, capillary refill < 2sec
- Normal pulse quality, no difference in central and peripheral pulses
- Warm extremities, blood pressure normal for age
- Urine output >1 mL/kg/h, normal mental status, CVP >8 mmHg

Laboratory

- Decreasing lactate
- SvO2 >70%

FURTHER READING

1. Feigin RD, Cherry JD. Feigin & Cherry's textbook of pediatric infectious diseases. Saunders/Elsevier, 2009.
2. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas and Bennett's Principles and Practice of infectious diseases, 8th ed, 2015, Elsevier Saunders

16.2 COMMON INFECTIOUS DISEASES IN CHILDREN

16.2.1 DIARRHEAL DISEASES

ACUTE DIARRHEA

- Acute diarrheal disease is the passage of loose, liquid or watery stool.
- Diarrhea is defined as passage of three or more loose or watery stools in 24-hour period.
- However, it is the recent change in consistency and character of stool than the number of stools that is more important.
- Its complications like dehydration, electrolytes disturbance and malnutrition are major causes of morbidity and mortality in developing countries.
- The leading cause of diarrhea in infants is the rotavirus followed by enteric adenoviruses.
- Shigella is a most common pathogen in children between 1 to 5 years with bloody diarrhea.
- Other bacterial pathogens include campylobacter, salmonella and Escherichia Coli.

Table 16. 3. Classification based on dehydration

Degree of dehydration	**Some**	**Severe**
a. Look for		
General condition	Restless, irritable	Lethargic, floppy, unconscious,
Eyes	Sunken	Deeply sunken and dry
Tears on cry	Absent	Absent
Mouth and tongue	Dry	Very dry
Thirst	Thirsty (drinks eagerly)	Very thirsty but (drinks poorly or unable to drink)
b. Feel for		
Skin pinch	Goes back slowly, takes 1 to 2 seconds	Goes back very slowly, takes more than 2 seconds
c. Decide	There is some dehydration (5-10% fluid loss).	There is severe dehydration (>10% fluid loss).
d. Treatment	Plan B With WHO recommended ORS solution to correct some dehydration.	Plan C With IV infusion urgently to correct severe dehydration and to prevent death

- **No dehydration:** if there are no enough signs to classify as "some" or "severe" dehydration. The degree of dehydration is less than 5 %.

I) Persistent diarrhea

- It can by classified based on duration:
    - **Severe persistent diarrhea**: If diarrhea lasts for 14 days or more and dehydration is present.
    - **Persistent diarrhea:** Diarrhea lasting for 14 days or more and there is no dehydration.

II) **Dysentery**

- Dysentery is a blood diarrheal stool.
- Dysentery can be an acute or persistent diarrhea and it can also be associated with dehydration.

Investigations

- Diagnosis is generally based on clinical profile.
- Stool examination or stool culture may be indicated in children with dysentery or persistent diarrhea but is not commonly needed for acute watery diarrhea.

TREATMENT

OBJECTIVES

- Prevent dehydration,
- Treat dehydration, when dehydration is present;
- Prevent nutritional damage, by feeding during and after diarrhea; and
- Reduce the duration and severity of diarrhea, and the occurrence of future episodes, by giving supplemental zinc.

PLAN A

- Give fluid and food to treat diarrhea at home.
    - If the child is being breastfed, advise the mother to breastfeed frequently and for longer at each feed.
    - If the child is exclusively breastfed, give ORS solution or clean water in addition to breast milk.

  - ○ After the diarrhea stops exclusive breastfeeding should be resumed, if appropriate to the child's age
  - ○ In non-exclusively breastfed children, give one or more of the following:
    - – ORS solution
    - – Food-based fluids (such as soup, rice water and yoghurt drinks)
    - – Clean water
- If the child cannot return to clinic, if diarrhea gets worse, teach the mother how to mix and give ORS and give the mother two packets of ORS to use at home.
- Show the mother how much fluid to give in addition to the usual fluid intake:
  - ○ Up to two years- 50 to 100 ml after each loose stool
  - ○ Two years or more: 100 to 200 ml after each loose stool
  - ○ Tell the mother to give frequent small sips from a cup
  - ○ If the child vomits, wait 10 minutes, then continue but more slowly. Continue giving extra fluid until the diarrhea stops.

DANGEROUS FLUIDS NOT TO BE GIVEN

- Drinks sweetened with sugar
- Commercial carbonated beverages
- Commercial fruit juices
- Sweetened tea
- Fluids with stimulant, diuretic or purgatives effects (e.g., coffee)
- Some medicinal teas or infusions

PLAN B

TREAT SOME DEHYDRATION WITH ORS IN CLINIC

- Give the recommended amount of ORS over 4-hour period

- Amount of Use the child's age only when you do not know the weight. The approximate ORS required (in ml) can be calculated by multiplying the child's weight (in kg) times 75.
- If the child wants more ORS than shown, give more
- If the child vomits, wait 10 minutes. Then continue, but more slowly.
- Continue breastfeeding whenever the child wants.

Table 16. 4. Amount of ORS to be given during the first 4 hours depending on age of the child

Age	Up to 4 months	4 Months up to 12 months	12 months up to 2 years	2 years up to 5 years
Weight	6 kg	6-10 kg	10-12 kg	12-19 kg
ORS in ml	200-400	400-700	700-900	900-1400

After 4 hours:

- Reassess the child and classify the child for dehydration.
- Select the appropriate plan to continue treatment.
- Begin feeding the child in clinic.

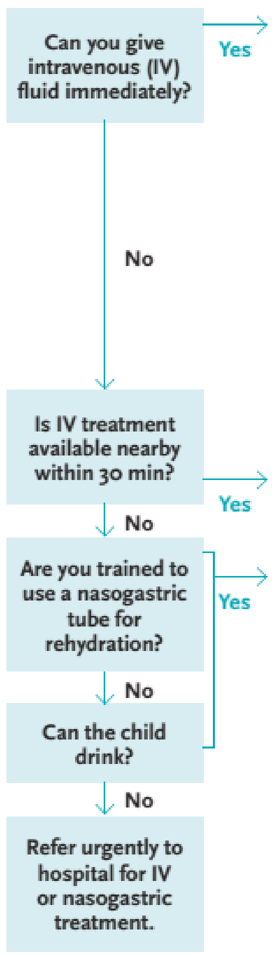
If the mother must leave before completing treatment

- Show her how to prepare ORS solution at home.
- Show her how much ORS to give to finish 4-hour treatment at home
- Give her enough ORS packets to complete rehydration. Also give her 2 packets as recommended in Plan A.
- Explain the 3 components of home treatment.

Treatment plan C: treat severe dehydration quickly

→ **Follow the arrows. If the answer is YES, go across. If NO, go down.**

START HERE



Can you give intravenous (IV) fluid immediately?

Yes

- Start IV fluid immediately. If the child can drink, give ORS by mouth while the drip is being set up. Give 100 ml/kg Ringer's lactate solution (or, if not available, normal saline), divided as follows:

Age	First give 30 ml/kg in:	Then give 70 ml/kg in:
Infants (< 12 months)	1 h[a]	
Children (12 months to 5 years)	30 min[a]	2.5 h

[a] Repeat once if radial pulse is still weak or not detectable

- Reassess the child every 15–30 min. If hydration status is not improving, give the IV drip more rapidly. Also watch for over-hydration.
- Also give ORS (about 5 ml/kg per h) as soon as the child can drink: usually after 3–4 h (infants) and 1–2 h (children).
- Reassess an infant after 6 h and a child after 3 h. Classify dehydration. Then choose the appropriate plan (A, B or C) to continue treatment.

No

Is IV treatment available nearby within 30 min?

Yes

- Refer **urgently** to hospital for IV treatment.
- If the child can drink, give the mother ORS solution, and show her how to give frequent sips during the trip.

No

Are you trained to use a nasogastric tube for rehydration?

No

Can the child drink?

Yes

- Start rehydration by tube (or mouth) with ORS solution: give 20 ml/kg per h for 6 h (total, 120 ml/kg).
- Reassess the child every 1–2 h:
  - If there is repeated vomiting or increasing abdominal distension, give the fluid more slowly.
  - If hydration status is not improving after 3 h, send the child for IV therapy.
- After 6 h, reassess the child and classify dehydration. Then, choose the appropriate plan (A, B or C) to continue treatment.

No

Refer urgently to hospital for IV or nasogastric treatment.

Note: If possible, observe the child for at least 6 h after rehydration to be sure the mother can maintain hydration by giving the child ORS solution by mouth.

PHARMACOLOGIC

- Antibiotics should not be used routinely.
  - They are reliably helpful only in children with bloody diarrhea, probable shigellosis, and suspected cholera with severe dehydration.

ZINC SUPPLEMENTS

- It has been shown that zinc supplements during an episode of diarrhea reduce the duration and severity of the episode and lower the incidence of diarrhea in the following 2-3 months.
- WHO recommends zinc supplements as soon as possible after diarrhea has started.
- Dose up to 6 months of age is 10 mg/day and age 6 months and above 20mg/day, for 10-14 days.

FURTHER READING

1. Haileamlak A. Why is the Acute Watery Diarrhea in Ethiopia attaining extended course? Ethiopian journal of health sciences. 2016;26(5):408.
2. IMNCI hand book

16.2.2 SEPSIS IN CHILDREN

BRIEF DESCRIPTION

- **Pediatric sepsis** is generally considered to comprise a spectrum of disorders that result from infection by bacteria, viruses, fungi, or parasites or the toxic products of these microorganisms.
- Early recognition and intervention clearly improve outcome for infants and children with conditions that lead to **sepsis**.

CAUSES

- Common pathogens in infant <1month of age
  - E. coli

  - Group B streptococci
  - Listeria monosytogens
- However, these pathogens can still be cause of sepsis up to 3 months of age

COMMON PATHOGENS IN OLDER CHILDREN

- Neisseria meningitides
- Streptococcus pneumonia
- Haemophilus influenza type b
- Staphylococcus aureus
- Group A streptococci
- Community acquired MRSA

HIGH-RISK GROUPS INCLUDE:

- Neonates
- Immuno-compromised children
- Children on prolonged broad spectrum antibiotic use
- ICU admissions
- Children with central venous access devices
- Children on immunosuppressive drugs

SEPTIC CHILDREN MAY PRESENT WITH:

- Cold shock characterized by a narrow pulse pressure and prolonged capillary refill. The underlying hemodynamic abnormality is septic myocardial dysfunction, which is more common in infants and neonates.
- Warm shock characterized by a wide pulse pressure and rapid capillary refill. The underlying hemodynamic abnormality is vasoplegia, which is more common in older children and adolescents.

CLINICAL MANIFESTATION

- Fever or hypothermia
- Tachycardia
- Tachypnea +/- hypoxia
- Altered state of consciousness
- Cold shock: narrow pulse pressure, prolonged capillary refill more in infant
- Warm shock: wide pulse pressure rapid capillary refill more common in older children and adolescent.

INVESTIGATION

- CBC with differential, CRP/ESR
- Urinalysis
- CSF analysis
- If it is available➔One set (2 bottles) of blood cultures (1 aerobic, 1 anaerobic, from 2 different sites), urinalysis and urine culture should be collected before the 1st dose of antibiotics

DIAGNOSIS OF SEPSIS

- Clinically, the Systemic Inflammatory Response Syndrome (SIRS) is the occurrence of at least two of the following criteria: **fever** >38.0°C or hypothermia <36.0°C, tachycardia, tachypnea, leucocytosis $>12*10^9$/l or leucopoenia $<4*10^9$/l.

TREATMENT

OBJECTIVE

- Early administration of empiric intravenous antibiotics (within 30-60min of presentation
- Empiric antibiotic recommendations may change based on evolving medical knowledge.
- Remove infectious source (catheter, drain abscess/fluid collections)

- Modify antibiotic based on culture results
- Carefully titrated fluid resuscitation
- Peripherally administered inotrope / vasopressor

Non-Pharmacologic

- Secure IV line,
- If the patient is in shock➔Initial fluid 20ml/kg of 0.9% N/S if needed 60ml/kg IV
- Consider blood transfusion if hemoglobin is less than 10mg/dl and FFP if the patient has high PT, PTT and INR.
- If the patient is in shock and has malnutrition
    - Volume is 15ml/kg 0.45%NS with 5% dextrose Or RL with 5% dextrose.
    - Can be repeated once if there is no sign of fluid overload

PHARMACOLOGIC

- The amount of fluid to be given depends on the cause of shock (febrile illness versus shock caused by GI loss, hemorrhage or any cause the depletes the intravascular volume), availability of Intensive care units in the specific set up, the degree of shock (normotensive/compensated or hypotensive/decompensated shock) and presence or absence of comorbidities like severe acute malnutrition and severe anemia.
- **If PICU is available**, give 40-60ml/kg crystalloids (10-20ml/kg per bolus) over the first hour with titration of fluid based on clinical parameters of cardiac output and discontinue the fluid if signs fluid overload develops.
- **If PICU is not available**, in children with shock (fulfilling all the three WHO criteria for shock cold extremities, fast weak pulse, and prolonged capillary refill time>3seconds) without hypotension may not benefit from fluid bolus can be put on maintenance fluid. But a subset of patients who develops the shock in the setting of causes which result in volume depletion (diarrhea, vomiting, bleeding, excessive diuresis) will benefit from the fluid bolus

- If there is no PICU but the child has hypotensive shock fluid bolus up to 40ml/kg (10-20ml/kg per bolus) in the first hour has to be give with titration base on clinical parameters of cardiac output. Stop the IV fluid if the patient develops signs of fluid overload.
- For children shock and malnutrition, 10-15ml/kg IV fluid over 1 hour.
    - If the patient improves after the first bolus, ReSomal can be continued via Nasogasrtic tube.
    - If the patient does not respond after the first bolus, consider transfusion with 10 ml/kg of cross matched blood slowly (over 3 hours)
- If the child has severe anemia (hemoglobin<5g/dl r hematocrit <15%) has shock, transfuse as soon as possible and give IV fluid only to maintain the normal hydration (maintenance fluid).
- Antibiotic should be started within an hour of initiating management for sepsis to cover the likely etiologic agents.
    - Age >1 month's Ceftriaxone or Cefotaxime 50-75mg/kg and Gentamycin 5mg/kg
    - For patients with septic shock (sepsis with CV organ dysfunction)
    - Inotrope/vasopressin Adrenaline/Noradrenaline 0.15Mic g/kg/hr (N/S 5%DW) 10 ml/hr. 0.05Micgram/kg/hr.
    - Respiratory support BiPAP, CPAP; If there is altered state consciousness intubation

FURTHER READING

1. Surviving Sepsis campaign international guideline, 2020
2. WHO pediatric ETAT guideline, 2016
3. Negussie A, Mulugeta G, Bedru A, Ali I, Shimeles D, Lema T, Aseffa A. Bacteriological profile and antimicrobial susceptibility pattern of blood culture isolates among septicemia suspected children in selected hospitals Addis Ababa, Ethiopia. *Int. J biolo. med research.* 2015 Nov; 6(1): 4709

16.2.3 PNEUMONIA IN CHILDREN

BACTERIAL PNEUMONIA

BRIEF DESCRIPTION

- Pneumonia defined as an acute infection and inflammation of lung parenchyma.
- WHO recommends diagnosis of pneumonia when children under five have acute on-set cough with tachypnea.
- There are two major types:
    - **Bronchopneumonia**: involves both the lung parenchyma and the bronchi. It is common in children and the elderly.
    - **Lobar pneumonia**: involves one or more lobes of the lung. It is common in young people

CAUSES

- Causative agents can be viral, bacterial or parasitic.
- Pathogens vary according to age, patient's condition and whether infection was acquired in the community or hospital (Gram negative are more common in hospital).
    - Neonates: group B streptococcus, Klebsiella, E.coli, Chlamydia and S. aureus
    - Children <5 years: Pneumococcus, Haemophilus influenzae, less frequently: S. aureus, M. catarrhalis, M. Pneumoniae, viruses (RSV, influenza, measles)
    - Children and adult >5 years: most commonly S.pneumoniae, followed by atypical bacteria, e.g. Mycloplasma pneumoniae, viruses
    - Immunosuppressed: Pneumocystis (in HIV infected)

PREDISPOSING FACTORS

- Malnutrition, lack immunization

- Rickets, preceding upper respiratory tract infection
- Exposure to cigarette smokers, indoor air pollution
- Immunosuppression (HIV, cancer, alcohol dependence)
- Measles, pertussis, preexisting lung or heart disease, diabetes

CLINICAL FEATURES

- According to the WHO 2013 guideline and national IMNCI guideline classification, a child presenting with cough or difficult breathing is classified as having severe pneumonia, pneumonia or no pneumonia (cough or cold).

SEVERE PNEUMONIA:

- Cough or difficult breathing
- Lower chest in drawing,
- Nasal flaring,
- Grunting in young infants.
- Fast breathing or abnormal breath sounds may also be present.

Pneumonia:

- Cough
- Fast breathing
- But no signs for severe pneumonia

No pneumonia:

- Cough or cold, if no sign for pneumonia or severe pneumonia.

Investigations

- o The decision to treat a child who has pneumonia is usually made clinically
- o Do a Chest X ray and look for complications
- o Sputum: For Gram stain, Ziehl-Neelsen (ZN) stain, culture for AFB

  - Blood: Complete blood count

PNEUMONIA IN AN INFANT (UP TO 2 MONTHS)

- Consider all children < 2 months with pneumonia as SEVERE disease.

Clinical features

- Rapid breathing (≥60 breaths/minute)
- Severe chest in drawing, grunting respiration
- Inability to breastfeed
- Stridor in a calm child, wheezing
- Fever may or may not be present
- Cyanosis and apnoeic attacks (SpO2 less than 90%)

Management

- Admit, keep baby warm
- Prevent hypo glycaemia by breastfeeding/giving expressed breast milk/ NGT
- If child is lethargic, do not give oral feeds. Use IV fluids with care
- Give oxygen to keep SpO2 >94%
- Antibiotics: Ampicillin + Gentamycin
  - **Dose**:
    - Ampicillin is 50mg/kg IV Q12 for those <14days old, QID for those > 14 days, for sepsis,
    - For meningitis 150mg/kg/dose BID for those <14 days old, 100mg/k/dose QID for >14 days;
    - Gentamicin 5 mg/kg IV once daily
    - In severely ill infants Ceftriaxone 100 mg/kg IV once daily
  - **Duration**

  - Continue treatment for at least 7 days
  - If septicemia is suspected, continue for 10 days
  - If meningitis is suspected, continue for 21 days.

16.2.4 PNEUMONIA IN A CHILD OF 2 MONTHS-5 YEARS

CLINICAL FEATURES

- Fever, may be high, low grade or absent (in severe illness)

Pneumonia

- Cough
- Fast breathing (2-12 months: ≥ 50 bpm, 1-5 years: ≥ 40 bpm)
- Mild chest wall in-drawing

SEVERE PNEUMONIA

Clinical features

- As above plus at least one of the following
  - Central cyanosis (blue lips, oral mucosa, finger nails or oxygen saturation < 90% using a pulse oximeter)
  - Inability to feed, vomiting everything
  - Convulsions, lethargy, decreased level of consciousness
  - Severe respiratory distress (severe chest in drawing, grunting, nasal flaring)
  - Extra pulmonary features, e.g., confusion or disorientation, may predominate and may be the only signs of pneumonia in malnourished or immunosuppressed children

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Prevent respiratory failure
- Prevent complications

NON-PHARMACOLOGIC

- Soothe the throat; relieve the cough with a safe remedy
- Safe remedies to recommend include:
- Breast milk for exclusively breast-fed infant
- Home fluids such as tea with honey, fruit juices
- Give oxygen if SpO2 < 90% with nasal prongs and monitor through pulse oximetry for those in respiratory distress via nasal cannula
- Gentle suction of thick secretions from upper airway

Pharmacologic

Antipyretic

- **Paracetamol**, 10-15mg /kg P.O., up to 4-6 times a day for the relief of high fever

Alternatives

- **Ibuprofen**, 5 – 10mg/kg/dose every 6 – 8hr P.O. (max. 40mg/kg/24hours).

Non-severe pneumonia

- **Antibiotic**

First-line

- **Amoxicillin**, 30-50mg/kg every 12hourss P.O for 5 days

Alternatives

- **Azithromycin**, 10mg/kg/24 P.O., once daily for 3 days mainly on patients have afebrile pneumonia syndrome.
- **Reassess child for progress after 3 days**

SEVERE PNEUMONIA

- **Benzyl penicillin,** 50,000units/kg/24hours IV QID for at least 3 days
- **N.B.** When the child improves switch to oral Amoxicillin: 30-50mg/kg/24 hours 3 times a day. The total course of treatment is 5-7days.
- If the child doesn't improve within 48 hours, switch to ceftriaxone 80mg/Kg/24 hours IM/IV for 5 days
- If staphylococcus is suspected (empyema, pneumatocele at X ray), give gentamicin 5 mg/kg once daily plus cloxacillin 50 mg/kg IV every 6-hour
- **Zinc** supplementation in children <5years with severe pneumonia

ATYPICAL PNEUMONIA

- It is a mild form of pneumonia that can be life threatening for some people.
- The illness is rare in children younger than 5 years old.

Causes

- Viruses or bacteria can cause atypical pneumonia.
- The most common cause of the illness in school-aged children is the bacteria Mycoplasma pneumoniae. It also causes bronchitis and chest colds.

Clinical features

- Fever, often low grade, Tiredness (fatigue), headache
- Skin rash, general feeling of sickness
- Cough, dry to phlegmy ear infections
- Croup, sinus infection, sore throat
- Wheezing in children who have an airway problem such as asthma
- These symptoms may appear anywhere from 1 to 4 weeks after exposure to the viruses or bacteria. They may last from a week to a month.

Diagnosis

- Clinical.

- Some time may need a chest X-ray and CBC

Treatment

- Treatment also depends on the cause of the illness.
- Antibiotics if the infection is from the bacteria.
- If the illness is from a virus, then antibiotics won't work.

Non- pharmacologic

- **Relaxes.** Stay at home from school until symptoms get better.
- **Drinks plenty of fluids.** Water, soups, and warm tea can help prevent dehydration.
- A humidifier can help with breathing problems.

Pharmacologic

- **Paracetamol for** fever or pain.
- **Azithromycin,** 10mg/kg P.O., on day 1, 5mg/kg on day 2-5, for children <6 months of age 10mg/kg/day for 5 days

ASPIRATION PNEUMONIA

BRIEF DESCRIPTION

- Aspiration pneumonia is a complication of pulmonary aspiration.

CLINICAL FEATURES

- Chest pain, fever, shortness of breath, wheezing, fatigue
- Blue discoloration of the skin
- Cough possibly with green sputum, blood or foul odor
- Bad breath
- Excessive seating
- Physical exam, such as a decreased flow of air, rapid heart rate, and a crackling sound in lungs.

RISK FACTORS

- Pneumonia from aspiration can occur when the defenses are impaired. This impairment may be due to:
    - Neurological disorders
    - Use of sedatives or anesthesia
    - Aweakened immune system
    - Esophageal disorders
    - Dental problems that interfere with chewing or swallowing
- Impaired consciousness
- Lung disease, seizure, stroke, dental problems
- Impaired mental status, swallowing dysfunction
- Gastroesophageal reflux diseases (GERD)

DIAGNOSIS

- High index of suspicion with the following investigation
    - CXR PA and Lateral, CBC
    - If it is available bronchoscopy and CT scan may be needed

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Prevent respiratory failure
- Prevent complications

Non-pharmacologic

- Give oxygen if SpO2 < 90% with nasal prongs and monitor through pulse oximetry for those in respiratory distress via nasal cannula
- Gentle suction of thick secretions from upper airway

Pharmacologic

- Ceftriaxone 80mg/Kg/24 hours IM/IV + Metronidazole 7.5mg/kg every 8 hours
- Refer the patient for possible removal

HOSPITAL AND VENTILATOR ASSOCIATED PNEUMONIA (HAP)

BRIEF DESCRIPTION

- New respiratory symptoms (cough, dyspnea, purulent sputum), fever and/or leukocytosis in a patient admitted for >48 hours. Chest x-ray or scan with a NEW pulmonary infiltrate (admitted >48h)

CLINICAL FEATURES

- Similar with bacterial pneumonia

CAUSES

- Frequent etiologies of HAP: Enterobacteriaceae, *Pseudomonas*, *Acinetobacter*, other GNR, *S aureus*

DIAGNOSIS AND INVESTIGATIONS

- Sputum/Endotracheal secretions to send to micro lab for gram stain and culture
- If it is available: blood culture x2 (please collect from 2 different sites)

TREATMENT

- **Patients at lower risk of drug resistant organisms, ie those with:** No IV antibiotics within previous 3 months, no structural lung damage, few or no co-morbidities, not known MRSA carriers
    - Ceftazidime Total daily dose 75 mg/kg IV (divided into 2 doses per day) AND
    - Gentamicin 3 – 5 mg/kg/day IV (given once daily) for 7 days

- **Patients at higher risk of drug resistant organisms, i.e. those with:** history of IV antibiotic use within previous 3 months**,** structural lung damage (Bronchiectasis, COPD, lung fibrosis), prior co-morbidities (cancer, advanced liver or renal disease, immunocompromised), known MRSA carrier
    - Piperacillin-Tazobactam 100 mg/kg IV q 8 hours for 7 day

FURTHER READING

1. Markos Y, Dadi AF, Demisse AG, Ayanaw Habitu Y, Derseh BT, Debalkie G. Determinants of under-five pneumonia at Gondar University hospital, Northwest Ethiopia: an unmatched case-control study. Journal of environmental and public health. 2019 Sep 23;2019.
2. Walker CL, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, O'Brien KL, Campbell H, Black RE. Global burden of childhood pneumonia and diarrhoea. The Lancet. 2013 Apr 20;381(9875):1405-16.

16.2.5 PLEURAL EFFUSION AND EMPYEMA

BRIEF DESCRIPTION

- Pleural effusions are a common finding in patients with pneumonia.
- More than 40% of patients with bacterial pneumonia and 60% of patients with pneumococcal pneumonia develop parapneumonic effusions.
- While treatment with antibiotics leads to resolution in most patients, some patients develop a more fibrinous reaction, with the presence of frank pus in the most severe cases. The latter is referred to as an empyema or empyema thoracis.
- Empyema thoracis: This develops as frank pus accumulates in the pleural space.

ETIOLOGY

- Virtually any type of pneumonia (e.g., bacterial, viral, atypical) can be associated with a parapneumonic pleural effusion.

- However, the relative incidence of parapneumonic pleural effusions varies with the organism.
- Viral pneumonia and Mycoplasma pneumonia cause small pleural effusions in 20% of patients.
- For thoracic empyema, bacterial pneumonia is the cause in 70%.

RISK FACTORS

- Risk factors for empyema thoracis include age (children), debilitation, pneumonia requiring hospitalization, and comorbid diseases, such as bronchiectasis, diabetes and gastroesophageal reflux disease.

LABORATORY STUDIES

- The presence of pleural fluid may be suggested based on physical examination findings; however, small pleural effusions may not be detected during the physical examination.

CHEST RADIOGRAPHY

- In this case, any significant effusion can be visualized using 2-view (ie, posteroanterior, lateral) chest radiography. Lateral chest radiography usually demonstrates the presence of a significant amount of pleural fluid.
- Sputum should be submitted for culture, especially if purulent
- The infecting organism may be suggested based on Gram stain results. Mixed florae are often seen in anaerobic infections.
- As with any infection, leukocytosis may be present (>12,000/μL) however, it should decrease with adequate antibiotic therapy.
- Diagnosing a complicated parapneumonic effusion and/or empyema is crucial for optimal management because a delay in drainage of the pleural fluid substantially increases morbidity.
- Ultrasonography can be used to localize fluid for a thoracentesis. Fluid appears dark or black on ultrasound images, and most bedside ultrasonography devices permit measurement of the depth of location

from the chest wall.

- Complex fluid (purulent or viscous) may have more density or shadows within in the pleural fluid collection. Sometimes, fibrinous strands can be seen floating in the pleural fluid.

OTHER TESTS

- While no diagnostic serum laboratory tests are available for a parapneumonic effusion, serum total protein and lactic dehydrogenase (LDH) levels should be obtained to help characterize whether the pleural fluid is an exudate or transudate. The ratio of pleural fluid/serum protein and LDH is used to distinguish between these two entities.

PROCEDURES

- Thoracentesis is recommended when the suspected parapneumonic pleural effusion is greater than or equal to 10 mm thick on a lateral decubitus chest radiograph.

PLEURAL FLUID STUDIES

- Blood cell count (WBC count) and differential: Results generally are not diagnostic, but most transudates are associated with a WBC counts of less than 1000 cells/μL and empyemas are exudates, with WBC counts generally greater than 50,000 cells/μL.
- Pleural fluid total protein, LDH, and glucose (corresponding serum protein and LDH): Exudates are defined by pleural/serum total protein ratio of greater than 0.5 and a pleural/serum LDH ratio of greater than 0.6 or a pleural fluid LDH value greater than two thirds the upper limit of normal. One criterion is sufficient to classify fluid as an exudate.
- Pleural fluid pH (iced blood gas syringe): Values of less than 7.20 are suggestive of a complicated pleural effusion.
- Other laboratories suggestive of complicated pleural effusion or empyema: These include (1) an LDH value of greater than 1000 U/L, (2) a pH of less than 7.00, and (3) a glucose level of less than 40 mg/dL.

MICROBIOLOGY (GRAM STAIN, BACTERIAL CULTURE)

- Acid-fast bacilli and fungal infections may cause pleural effusions or empyema, but these organisms are more difficult to culture from pleural fluid.

HISTOLOGIC FINDINGS

- Multiple granulocytes are typically identified on histologic examination. Necrotic debris may be present. Bacteria are seen in the pleural fluid in severe infections.

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

Chest tubes (tube thoracostomy)

- Insert chest tubes immediately after a complicated parapneumonic pleural effusion or empyema thoracis is diagnosed. The key to resolution involves prompt drainage of pleural fluid because delay leads to the formation of loculated pleural fluid.

Pharmacologic

- Selection of an appropriate antibiotic that will cover likely pathogens.
- For a patient with community-acquired pneumonia, the recommended agents are second- or third-generation cephalosporins in addition to a macrolide.
- For patients hospitalized with severe community-acquired pneumonia, initiate treatment with a macrolide plus a third-generation cephalosporin with anti-pseudomonal activity.

FURTHER READING

1. Eslami G, Panji A, Firoozi H, Hosseinzadeh F, Moradi S, Mohammadpour

Mir A, Rezai MS. The Survey of Pediatric Pleural Empyema in North of Iran (from 2004 to 2016). International Journal of Pediatrics. 2018 Mar 1;6(3):7421-32.

2. Ampofo K, Pavia A, Stockmann C, Blaschke AJ, Hersh AL, Thorell E, Sanderson SK, Rosen P, Korgenski EK, Daly JA, Byington CL. Changing trends in parapneumonic empyema (PPE) in the United States during the pneumococcal conjugate vaccines era. InOpen Forum Infectious Diseases 2015 Dec 1 (Vol. 2, No. suppl_1). Oxford University Press.

16.2.6 MENINGITIS IN CHILDREN

BRIEF DESCRIPTION

- Meningitis is acute inflammation of the meninges (the membranes covering the brain). Bacterial meningitis is a notify able disease.
- This is an acute and one of the most potentially serious infections in infants and children that affects the central nervous system.

CAUSES

- Most common bacterial: *S. pneumoniae. H. influenza type b (mainly in young children), N meningitides* and Enteric bacilli.
- Viral (HSV, enteroviruses, HIV, VZV etc.)
- Cryptococcus neoformans (in the immune-suppressed)
- Mycobacterium tuberculosis

CLINICAL FEATURES

- In infants whose cranial sutures are still open, budged fontanel
- Rapid onset of ever
- Vomiting
- Irritability, lethargy, convulsion, coma
- Bulging of the anterior fontanel

- Haemorrhagic rash (N. meningitidis infection)
- In older children focal neurologic signs, such as: A sixth nerve palsy, may be more prominent
- Signs of meningeal irritation, such as nuchal rigidity, kerning's sign or Brudziniski sign are usually present.

Differential diagnosis

- Brain abscess
- Space-occupying lesions in the brain
- Drug reactions or intoxications
- Cerebral malaria
- Viral meningitis
- Poisoning

Investigations

- CSF: Increased number of white cell count, low level of CSF glucose and elevated protein level are the usual findings. Indian-ink staining (for Cryptococcus), gram stain, culture and sensitivity will reveal the microorganism.
- Blood: For serological studies and full blood count
- Neuroimaging u/s of brain, CT or MRI
- Chest X-ray and ultrasound to look for possible primary site

Treatment

Objectives

- Decrease the risk of grave complications and mortality
- Avoid residual sequelae
- Shorten hospital stay

Non-pharmacologic

- Restrict fluid intake to 70% of calculated maintenance.
- Monitor urine output and daily weight
- Support feeding (NGT if necessary)
- Monitor vital signs

Pharmacologic

First line

- **Ceftriaxone**, 100mg/kg, IV once daily for 10 days for all cases

Alternative

- **Cefotaxime**, 225-300mg/kg/ day divided every 6 or 8 hrs

N.B. Antibiotic treatment may be modified when culture and sensitivity results are collected.

CAUSATIVE ORGANISMS IDENTIFIED

- Streptococcus pneumoniae (10 to 14-day course; up to 21 days in severe case)
- **Benzyl penicillin** 100,000 IU/kg per dose IV or IM every 4 hours or **ceftriaxone** 100 mg/kg daily dose IV or IM every 12 hours
- Haemophilus influenzae (10-day course) Ceftriaxone hours100 mg/kg per dose
- IV or IM every 12, only if the isolate is reported to be susceptible to the particular drug or **ampicillin** Child: 50 mg/kg per dose
- Neisseria meningitidis (5-7 day course)
- **Benzylpenicillin** 100,000-150,000 IU/kg every 6 hours Or Ceftriaxone 100 mg/kg daily dose

Note: Consider prophylaxis of close contacts (especially children < 5 years): Ceftriaxone 125mg IM stat.

- Listeria mono cytogenes (at least 3 weeks course)

  - Common cause of meningitis in neonates and immunosuppressed children
  - Ampicillin 50mg/kg IV every 6 hours.

Adjunct to treatment with antibiotics

- **Dexamethasone** 0.6mg/kg/day divided QID for two-four days in cases of suspected H. influenza meningitis.
  - It should be administered just before or with antibiotics

Note:

- Because of the potential severity of the disease, refer all patients to hospital after pre-referral dose of antibiotic.
- Carry out lumbar puncture promptly and initiate empirical antibiotic regimen

Prevention

- Avoid overcrowding
- Improve sanitation and nutrition
- Prompt treatment of primary infection (e.g., in respiratory tract)
- Immunization as per national schedules
- Mass immunization if N. Meningitis epidemic

FURTHER READING

1. Gudina EK, Tesfaye M, Wieser A, Pfister HW, Klein M. Outcome of patients with acute bacterial meningitis in a teaching hospital in Ethiopia: A prospective study. PLoS One. 2018 Jul 18;13(7):e0200067.
2. Tegene B, Gebreselassie S, Fikrie N. Bacterial Meningitis: a five year retrospective study among patients who had attended at University of Gondar Teaching Hospital, Northwest Ethiopia. Biomedical Research and Therapy. 2015 May 2;2(5):270-8.

16.2.7 URINARY TRACT INFECTION IN CHILDREN

ACUTE CYSTITIS

BRIEF DESCRIPTION

- An infection/inflammation involving the bladder, a part of the lower urinary tract.
- Uncomplicated cystitis is less common in men and needs to be differentiated from prostatitis and urethritis (sexually transmitted).

RISK FACTORS

- Age younger than 12 months
- White race
- Temperature above 39°C
- Illness for 2 days or more
- Absence of any other source for fever

CAUSE

- Bacterial infection, usually gram negative (from intestinal flora) e.g. Escherichia coli

CLINICAL FEATURES

- Dysuria (pain and difficulty in passing urine)
- Urgency of passing urine, frequent passing of small amounts of urine
- Suprapubic pain and tenderness
- Pyuria/haematuria (pus/blood in the urine making it cloudy)
- Foul smelling urine
- There may be retention of urine in severe infection

INVESTIGATIONS

- Midstream urine: urine analysis for protein, blood, leucocytes, nitrates, sediment
- Culture and sensitivity (if resistant/repeated infections)

DIAGNOSTIC CRITERIA

- Symptoms + leucocytes and/ or nitrates at urine analysis

Note: Asymptomatic bacteriuria or pyuria (leucocytes in urine) does not need treatment except in risk groups such as patients undergoing urological interventions and post kidney transplant patients

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complications

Non-pharmacologic

- Ensure high fluid intake

PHARMACOLOGIC

First line agents:

- Cotrimoxazole (4mg trimethoprim- 20mg sulfamethoxazole/kg every 12 hours) for 3-5 days

Alternatives

- Amoxicillin clavulanate 50-80mg Amoxicillin divided in to 3 doses per day for 3-5 days
- Ciprofloxacin 10 mg/kg 8-12 hourly for 3 days
- If poor response or recurrent infections: Refer for investigation of culture and sensitivity and further management

PREVENTION

- Improved personal/genital hygiene
- Drink plenty of fluids

ACUTE PYELONEPHRITIS

BRIEF DESCRIPTION

- Upper urinary tract infection involving one or both kidneys (but not usually involving the glomeruli)

CAUSE

- Bacterial infection, e.g. Escherichia coli, usually due to ascending infection (faecal-perineal-urethral progression of bacteria)

RISK FACTORS

- Bladder outlet obstruction
- Malformations of urinary tract
- HIV, diabetes

CLINICAL FEATURES

- Loin pain, tenderness in one or both kidney areas (renal angle)
- Fever, rigors (generalized body tremors)
- Vomiting
- If associated cystitis: dysuria, urgency, frequency
- Diarrhea and convulsions (common in children)
- In infants : may simply present as fever and poor feeding/disorientation without other signs

DIFFERENTIAL DIAGNOSIS

- Appendicitis
- Infection of the fallopian tubes (salpingitis)

- Infection of the gall bladder (cholecystitis)

INVESTIGATIONS

- Urine: Microscopy for pus cells and organisms, C&S of mid-stream urine
- Specimen should reach the lab within 2 hours of collection
- Blood: Full count, C&S, urea, electrolytes
- Ultrasound kidneys/prostate

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complications

Non-pharmacologic

- Ensure adequate intake of fluid (oral or IV) to irrigate bladder and dilute bacterial concentrations

PHARMACOLOGIC

- Give paracetamol 1 g every 6-8 hours for pain and fever
- Ceftriaxone 50-80 mg/kg IV once a day
- Following initial response to parenteral therapy: Consider changing to: Cefixime16 mg/kg the first day then 8 mg/kg to complete 10 days
- Alternative regimen: Combination of Ampicillin 50mg/kg/dose QID plus Gentamycin 7.5mg/kg daily is recommended
- Consider referral if there is no response in 72 hours and for children with recurrent infections (to exclude urinary tract malformations).

PREVENTION

- Ensure perianal hygiene
- Ensure regular complete emptying of the bladder and/or double voiding (additional attempt to empty bladder after initial urine flow ceases).

FURTHER READING

1. Pediatric hospital care: Ethiopia 2016
2. European urology society guideline, 2016
3. Hand book for the management of common renal problems, Ethiopia, 2009

16.2.8 OSTEOMYELITIS AND SEPTIC ARTHRITIS IN CHILDREN

OSTEOMYELITIS

BRIEF DESCRIPTION

- Skeletal infections are more common in infants and toddlers than in older children.
- The risk of permanent disability is increased if the growth plate of bone or the synovium is damaged.

CAUSES

- Bacteria are the most common pathogens in acute skeletal infections with S. aureus being the most common cause in all age groups including newborns.
- Risk factor: sickle cell disease (causative agent mostly S.Aureus, Salmonella also common).

CLINICAL FEATURES

ACUTE OSTEOMYELITIS

- Onset is usually over several days
- Earliest signs and symptoms may be subtle.
- Fever, usually high but may be absent, especially in neonates
- Pain (usually severe)
- Tenderness and increased "heat" at the site of infection, swelling of the

surrounding tissues and joint

- Reduced or complete loss of use of the affected limb. Neonates may exhibit pseudo paralysis or pain with movement of the affected extremity
- The patient is usually a child of 4 years or above with reduced immunity, but adults may also be affected
- History of injury may be given, and may be misleading, especially if there is no fever

CHRONIC OSTEOMYELITIS

- May present with pain, erythema, or swelling, sometimes in association with a draining sinus tract
- Deep or extensive ulcers that fail to heal after several weeks of appropriate ulcer care (e.g., in diabetic foot), and non-healing fractures, should raise suspicion of chronic osteomyelitis

DIFFERENTIAL DIAGNOSIS

- Infection of joints
- Injury (trauma) to a limb, fracture (children)
- Bone cancer (osteosarcoma, around the knee)
- Pyomyositis (bacterial infection of muscle)
- Cellulitis
- Sickle-cell disease (thrombotic crisis)

INVESTIGATIONS

- Diagnosis of osteomyelitis is generally clinical
- X-ray shows
    - Nothing abnormal in first 1-2 weeks
    - Loss of bone density (rarefaction) at about 2 weeks
    - May show a thin “white” line on the surface of the infected part of the

bone (periosteal reaction and lytic changes)

- Later, may show a piece of dead bone (sequestrum)
- Radionuclide scans are definitive and establish the diagnosis very early in the course.

- Blood: CBC, ESR, C&S: Type of bacterium may be detected

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Decrease the risk of complications
- Facilitate appropriate growth

Non-pharmacologic

1. Patients with suspected osteomyelitis need to be referred to hospital for appropriate management.
2. Immobilize and elevate the affected limb Surgical intervention may be indicated in the following cases:
3. Drainage of sub periosteal and soft tissue abscesses, and intramedullary purulence
   - Debridement of contiguous foci of infection (which also require antimicrobial therapy)
   - Excision of sequestra (i.e., devitalized bone)
   - Failure to improve after 48-72 hours of antimicrobial therapy

Pharmacologic

- Control pain with oral **paracetamol** 10mg/kg every 4 – 6 hours. If pain is not controlled with paracetamol, follow the analgesic ladder of pain management.
- **Cloxacillin** 50-100mg/kg/day divided every six hours for 3-6 weeks.

Or

- **Cefazolin** 30-40mg/kg Max Dose 2 gm daily for 3-6 weeks

Chronic osteomyelitis

- Surgery and antibiotics

PYOGENIC ARTHRITIS (SEPTIC ARTHRITIS)

BRIEF DESCRIPTION

- Acute infection, which is common in children affecting a single joint (usually a large joint).
- Usually, hematogenous spread from a primary focus following bacteremia (e.g., septic skin lesions, sinus infections, throat infections, abrasions, wounds, pressure sores, and osteomyelitis)

CAUSES

- Commonly involved in acute arthritis: Staphylococcus aureus and Gram-negative bacilli, e.g., Salmonella spp, Streptococcus spp, Gonococcus
- In chronic septic arthritis: Brucella, tuberculosis

CLINICAL FEATURES

- Swollen and warm joint
- Severe pain, reduced or abolished movement, temporary loss of limb function (pseudoparalysis)
- Localized heat and tenderness
- Systemic symptoms: fever (neonates may not show fever but refuse to feed), general malaise
- Complications: irreversible joint damage if immediate treatment is not established

DIFFERENTIAL DIAGNOSIS

- Inflammatory joint disease
- Intra-articular hemorrhage, e.g., hemophilia and other bleeding disorders

- Trauma
- Osteomyelitis of neighboring bone

INVESTIGATIONS

- Blood: Full blood count, C&S, ESR (usually elevated)
- Joint fluid: Aspirate for C&S; in case of failure to get pus by aspiration, use arthrotomy (in theatre)
- Joint fluid: Gram stain

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Decrease the risk of complications
- Facilitate appropriate growth

Non-pharmacologic

- Immobilize and elevate the affected limb, try splinting

Pharmacologic

- Control pain with oral **paracetamol** 10mg/kg every 4 – 6 hours.
- If pain is not controlled with paracetamol, give Ibuprofen or follow the analgesic ladder of pain management.
- **Cloxacillin**, 50-100mg/kg/day divided every six hours for 3-6 weeks

Alternative:

- **Cefazolin** 1st gen cephalosporin: 30-40mg/kg Max Dose 2 gm daily for 3-6 weeks
- REFER URGENTLY to hospital Aspirate articular fluid for gram stain, and C&S if available (use local skin and subcutaneous anesthesia if indicated)
- Repeat daily until no further pus is obtained Or open drainage in theatre

- In children with gram negative at gram stain, negative stain or adolescent with suspicion of gonococcal add Ceftriaxone 75mg/kg /day IV

FURTHER READING

1. Feigin RD, Cherry JD. Feigin & Cherry's textbook of pediatric infectious diseases. Saunders/Elsevier; 2009.
2. Van Schuppen J, van Doorn MM, van Rijn RR. Childhood osteomyelitis: imaging characteristics. Insights into imaging. 2012 Oct 1;3(5):519-33.

16.2.9 MEASLES

BRIEF DESCRIPTION

- An acute, highly communicable viral infection characterized by a generalized skin rash, fever, and inflammation of mucous membranes.
- Measles is a notifiable disease.

CAUSE

- Measles virus spreads by droplet infection and direct contact

CLINICAL FEATURES

- Catarrhal stage: high fever, Koplik's spots (diagnostic) runny nose, barking cough, and conjunctivitis
- Misery, anorexia, vomiting, diarrhea
- Later: generalized maculopapular skin rash followed by desquamation after few days

COMPLICATIONS

- Secondary bacterial respiratory tract infection, e.g. bronchopneumonia, otitis media
- Severe acute malnutrition especially following diarrhea
- Cancrum oris (from mouth sepsis)

- Corneal ulceration and panophthalmitis – can lead to blindness
- Demyelinating encephalitis
- Thrombocytopaenic purpura Other complications
- Subscute sclerosing panencephalitis (SSPE)
- Myocarditis

DIFFERENTIAL DIAGNOSIS

- German measles (Rubella)
- Other viral diseases causing skin rash

INVESTIGATIONS

- Clinical diagnosis is sufficient though virus isolation is possible
- Case definition: Patient with 3C(Cough, coryza, conjunctivitis) and generalized maculo- papular rash

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Isolate patients (at home or health center)
- Increase fluid and nutritional intake (high risk of malnutrition and dehydration)

Pharmacologic

- Paracetamol prn for fever
- Apply tetracycline eye ointment 1% every 12 hours for 5 days
- Give 3 doses of vitamin A: first dose at diagnosis, 2nd dose the next day and 3rd dose on day 14

  - Child <6 months: 50,000 IU
  - Child 6-12 months: 100,000 IU
  - Child >12 months: 200,000 IU
- Monitor for and treat secondary bacterial infections with appropriate antibiotics immediately
- Refer to hospital in case of complications

Prevention

- Measles vaccination
- Avoid contact between infected and uninfected persons
- Educate the public against the common local myths e.g. stopping to feed meat and fish to measles patients

FURTHER READING

1. Poletti P, Parlamento S, Fayyisaa T, Feyyiss R, Lusiani M, Tsegaye A, Segafredo G, Putoto G, Manenti F, Merler S. The hidden burden of measles in Ethiopia: how distance to hospital shapes the disease mortality rate. BMC medicine. 2018 Dec;16(1):1-2.
2. Nandi A, Shet A, Behrman JR, Black MM, Bloom DE, Laxminarayan R. Anthropometric, cognitive, and schooling benefits of measles vaccination: Longitudinal cohort analysis in Ethiopia, India, and Vietnam. Vaccine. 2019 Jul 18;37(31):4336-43.

16.2.10 MUMPS

BRIEF DESCRIPTION

- Mumps is a contagious disease caused by a filterable virus.
- The parotid glands are the salivary glands most commonly involved with mumps, but the sublingual and submandibular glands may also be affected.
- In 75-80% of cases both glands are involved.

CLINICAL FEATURES

- Swelling of the involved gland.
- Redness and slight swelling of the opening of the duct.
- Displacement of the auricle.
- The secretions are not purulent.
- There is no fever

Investigations

- Diagnosis is clinical

TREATMENT

OBJECTIVES

- Relieve symptoms

Non pharmacologic

- Massage the gland
- Decrease spread of infection to other contacts
- Isolation of patients with mumps: for 5 days

PHARMACOLOGIC

Paracetamol, 30 - 40mg/kg/24 hr. divided into 4 – 6 doses for children

FURTHER READING

1. Hviid A, Rubin S, Mühlemann K. Mumps. The Lancet. 2008 Mar 15;371(9616):932-44.
2. Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C. Vaccines for measles, mumps and rubella in children. Evidence-Based Child Health: A Cochrane Review Journal. 2013 Nov;8(6):2076-238.

16.2.11 PERTUSSIS (WHOOPING COUGH)

BRIEF DESCRIPTION

- Pertussis or Whooping cough is a highly contagious clinical syndrome characterized by an inspiratory whoop following paroxysmal cough.
- History of similar illness in the vicinity is an important evidence for diagnosis with incubation period of 7-10days.
- Appropriate and timely vaccination is protective.

CLINICAL FEATURES

Stage 1: Coryzal (catarrhal: 1-2 weeks)

- Most infectious stage
- Nonspecific upper respiratory tract symptoms including runny nose mild cough and low-grade fever.

Stage 2: Paroxysmal (1-6weeks)

- More severe and frequent repetitive coughs followed by an inspiratory whoop
- The child is well and playful between paroxysms of cough
- Post tussive vomiting, conjunctival hemorrhage
- Cyanosis, occasionally after a paroxysm of cough
- Fever may be present; patient becomes increasingly tired
- In infants <6 months: paroxysm led to apnoea, cyanosis (coughing bouts and whoops may be absent)

Stage 3: Convalescent stage (4-6weeks)

- Paroxysmal symptoms reduce over weeks or months
- Cough may persist

COMPLICATIONS MAY INCLUDE:

- **Respiratory**: pneumonia (new onset fever a symptom) atelectasis, emphysema, bronchiectasis, otitis media

- **Nervous system**: convulsions, coma, intracranial hemorrhage
- **Others**: malnutrition, dehydration, inguinal hernia, rectal prolapse

DIFFERENTIAL DIAGNOSIS

- Chlamydial and bacterial respiratory tract infection
- Foreign body in the trachea

INVESTIGATIONS

- Diagnosis of pertussis is entirely based on clinical grounds and presence of similar illness in the vicinity.
- Chest X-ray may show para cardiac infiltrates and may be helpful in suggesting comorbid conditions
- White blood cell count may be elevated

TREATMENT

OBJECTIVES

- Relieve symptoms
- Avoid complications

Non-pharmacologic

- Maintain nutrition and fluids
- Give oxygen and perform suction if the child is cyanotic
- For the unimmunized or partly immunized, give PENTA (three doses) as per routine immunization schedule
- Isolate the patient (avoid contact with other infants) until after 5 days of antibiotic treatment

Pharmacologic

First line

- **Erythromycin**, 12.5mg/kg P.O., QID for ten days

Alternatives

- **Clarithromycin**, 15 – 20mg/kg/24hours, P.O., divided in to two doses for 7 days

  OR

- **Azithromycin**, 10mg/kg/24hours, P.O. for 5 days

Prevention

- Isolation
- Treatment of contact

FURTHER READING

1. Gopal DP, Barber J, Toeg D. Pertussis (whooping cough). bmj. 2019 Feb 22;364.
2. Alamaw SD, Kassa AW, Gelaw YA. Pertussis outbreak investigation of Mekdela district, South Wollo zone, Amhara region, North-West Ethiopia. BMC research notes. 2017 Dec 1;10(1):420.

16.2.12 POLIO MYELITIS (ACUTE FLACCID PARALYSIS)

BRIEF DESCRIPTION

- An acute viral infection characterized by acute onset of flaccid paralysis of skeletal muscles. It is transmitted from person to person through the faecal-oral route.
- Poliomyelitis is a notify able disease.

CAUSE

- Polio virus (enterovirus) types I, II, and III

CLINICAL FEATURES

- Majority of cases are asymptomatic, only 1% result in flaccid paralysis
- Non paralytic form: minor illness of fever, malaise, headache, and vomiting, muscle pains, spontaneous recovery in 10 days
- Paralytic form: after the specific symptoms, rapid onset (from morning to evening) of asymmetric flaccid paralysis, predominantly of the lower limbs, with ascending progression
- Paralysis of respiratory muscles is life threatening (bulbar polio)
- Aseptic meningitis may occur as a complication

DIFFERENTIAL DIAGNOSIS

- Guillain-Bars. Syndrome
- Traumatic neuritis
- Transverse myelitis
- Pesticides and food poisoning

NB: Consider all case of Acute Flaccid Paralysis as possible Poliomyelitis: alert the district focal person for epidemic control, and send 2 stool samples (refrigerated).

Investigations

- Isolation of the virus from stool samples
- Viral culture

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

Acute stage

- Poliomyelitis in this stage without paralysis is difficult to diagnose

Paralytic form

- If paralysis is recent, rest the patient completely

Note: Do not give IM injections as they make the paralysis worse

- Refer the patient to a hospital for supportive care
- After recovery (if partially/not immunized), complete recommended immunization schedule

CHRONIC STAGE

- Encourage active use of the limb to restore muscle function/physiotherapy
- In event of severe contractures, refer for corrective surgery

PREVENTION

- Isolate patient for nursing and treatment, applying contact and droplets precautions
- Immunize all children below 5 years from the area of the suspected case
- If case is confirmed, organize mass immunization campaign
- Proper disposal of children's faeces
- Proper hygiene and sanitation

FURTHER READING

1. World Health Organization. PERFORMANCE OF ACUTE FLACCID PARALYSIS (AFP) SURVEILLANCE AND INCIDENCE OF POLIOMYELITIS, 2013 (DATA RECEIVED IN WHO HEADQUARTERS AS OF 20 AUGUST 2013). Weekly Epidemiological Record= Relevé épidémiologique hebdomadaire. 2013;88(36):385-8.
2. Cowger TL, Burns CC, Sharif S, Gary Jr HE, Iber J, Henderson E, Malik F, Zahoor Zaidi SS, Shaukat S, Rehman L, Pallansch MA. The role of supplementary environmental surveillance to complement acute flaccid paralysis surveillance for wild poliovirus in Pakistan–2011–2013. PLoS One. 2017 Jul 25;12(7):e0180608.

16.2.13 VARICELLA (CHICKEN POX)

BRIEF DESCRIPTION

- A highly contagious viral infection. Patients are contagious from 2 days before onset of the rash until all lesions have crusted.
- An attack of chicken pox establishes a lifelong latent infection of sensory neural ganglions.
- Disease is more severe and complicated in adults.

CAUSES

- Varicella Zoster virus (VZV) by droplet infection

CLINICAL FEATURES

- Incubation period is 14 days, but shorter in immunocompromised host
- Mild fevers occur 10-20 days after exposure
- Prodromal symptoms consisting of low fever, headache, and malaise occurring 2 to 3 days before the eruption
- Eruptive phase: they appear as macules, papules, vesicles pustules and crusts. The most characteristic lesion is a vesicle looking like a drop of water on the skin. Vesicles rupture easily and may become infected
- The rash begins on the trunk and spreads to the face and extremities
- Lesions of different stages (crops) exist together at the same time in any given body area
- Complications may include septicaemia, pneumonia, fulminating haemorrhagic varicella, and meningoencephalitis

DIFFERENTIAL DIAGNOSIS

- Drug-induced eruption
- Scabies
- Insect bites

- Erythema multiforme, impetigo
- Other viral infections with fever and skin rash

INVESTIGATIONS

- Virus isolation possible but not necessary
- Diagnosis is practically clinical

TREATMENT

OBJECTIVES

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Symptomatic and supportive treatment
- Apply calamine lotion every 12 hours
- Cool, wet compresses to provide relief
- Keep child at home/remove from school till healed to avoid spread

Non-pharmacologic

- Chlorpheniramine: Child >5 years: 1-2 mg every 12 hours for 3 days
- Pain relief: paracetamol 10 mg/kg every 6 hours
- In children >12 years consider antivirals: Oral acyclovir 800 mg every 6 hours for 7 days

Prevention

- Isolation of infected patient
- Avoid contact between infected persons and immunosuppressed persons

FURTHER READING

1. Macartney K, Heywood A, McIntyre P. Vaccines for post-exposure prophylaxis against varicella (chickenpox) in children and adults. Cochrane Database of Systematic reviews. 2014(6).

16.2.14 MALARIA IN CHILDREN

BRIEF DESCRIPTION

- Malaria is a major public health problem in Ethiopia and has been consistently reported as one of the leading causes of morbidity and mortality.
- Malaria is a parasitic infection caused by plasmodium species known to affect humans.
- The most serious and life-threatening disease occurs from Plasmodium Falciparum infection.
- Prompt diagnosis and treatment is essential even in mild cases to prevent complications.

CAUSES:

- the commonest causes of Malaria in Ethiopia are P. Falciparum and P. vivax

CLINICAL FEATURE: UNCOMPLICATED MALARIA

- Fever 38°C, chills, rigors, sweating, severe headache, flu-like symptoms
- Generalized body and joint pain
- Nausea and or vomiting, loss of appetite
- Abdominal pain (especially in children), splenomegaly
- Irritability and refusal to feed (in infants)

INVESTIGATIONS AND DIAGNOSIS

- Microscopy - thick and thin blood films for malaria parasites
- Rapid diagnostic tests (RDT) - if microscopy is unavailable
- CBC
- The diagnosis of malaria can be confirmed when malaria parasites are demonstration in the blood films (thick or thin) or with Rapid Diagnostic Test (RDT).
- Blood film is also helpful to estimate the degree of parasitemia, which

is extremely useful not only to predict severity but gauge response to treatment as well.

- If neither microscopy nor rapid tests are available, diagnosis should be made on the basis of clinical symptoms.

NOTE: Clinical diagnosis of malaria is made in a patient who has fever or history of fever in the last 48 hours and lives in malaria-endemic areas or has a history of travel within the last 30 days to malaria-endemic areas. Malaria treatment based on clinical diagnosis must be the last option when there is no RDT or blood film microscopy

TREATMENT

OBJECTIVES

- Treat the patient and restore quality of life and productivity
- Prevent uncomplicated malaria from progressing to severe and fatal illness
- Prevent death from malaria complication
- Prevent the development and transmission of drug resistance
- Decrease malaria transmission to others

Non-pharmacologic

- Apply tepid sponging or fanning to reduce body temperature
- Admit or refer severe complicated cases

Pharmacologic

- **Treatment of uncomplicated *P. Falciparum malaria***

First line

- **Artemether + Lumefantrine,** 20mg + 120mg in a fixed dose combination

N.B. Artemether-lumefantrine should not be used as malaria prophylaxis either alone or in combination;

Table 16. 5. Dose regimens of artemether-lumefantrine

Weight (KG)	Age	Dose
5-14 kg	From 4 months to 2 years	1 tablet bid for 3 days
15-24 kg	From 3 years to 7 years	2 tablets bid for 3 days
25-34 kg	From 8 years to 10 years	3 tablets bid for 3 days
>35 kg	10 years & above	4 tablets bid for 3 days

Alternative

- **Quinine dihydrochloride**, 10 mg quinine sulphate salt/kg TID for 7 days.

Treatment of uncomplicated *P. Vivax* malaia

- **Chloroquine phosphate,** 1 g, then 500 mg in 6 hours followed by 500 mg p.o. QD for 2 days, or 1 g at 0 and 24 hours followed by 0.5 g at 48 hours P.O.

Followed by

- **Primaquine,** 15mg base P.O. QD for 14 days.

Alternatives

- **Artemether + Lumefantrine,** 20mg + 120mg in a fixed dose combination

  OR

- **Quinine dihydrochloride**, 10 mg quinine sulphate salt/kg TID for 7 days

Treatment of uncomplicated mixed infection (Multi-species RDT positive for *P. falciparum* and *P. vivax*)

First line

- **Artemether + Lumefantrine,** 20mg + 120mg in a fixed dose combination

Alternative

- **Quinine dihydrochloride**, 10 mg quinine sulphate salt/kg TID for 7 days

COMPLICATED P. FALCIPARUM MALARIA

- Delay in diagnosis or inappropriate treatment of uncomplicated malaria can lead to the rapid development of severe or 'complicated malaria'." It mostly occurs in children under 5 years of age and non-immune individuals. Severe malaria may lead to death unless it is diagnosed early and appropriately managed.

CLINICAL FEATURES

- Inability to take in fluids (or breast milk in children), repeated profuse vomiting
- Hemoglobinuria Dark or 'cola-colored' urine, oliguria, renal failure
- Generalized weakness, inability to walk or sit without assistance
- Sleepiness, change of behavior, repeated generalized convulsions, altered consciousness, confusion, delirium, convulsions, coma
- Difficulty in breathing, tachypnoea, respiratory distress and/or cyanosis, crepitations on chest examination
- Hypoglycemia, severe anemia (Hb < 6 g/dL)
- Hyperpyrexia (axillary temperature >38.5°C)
- Circulatory collapse or shock (cold limbs, weak rapid pulse)
- Spontaneous unexplained heavy bleeding (disseminated intravascular coagulation)

INVESTIGATIONS AND DIAGNOSIS

- Microscopy - thick and thin blood films for malaria parasites
- Rapid diagnostic test (RDT) - if microscopy is unavailable
- CBC, RBS, Blood grouping and cross-matching
- BUN and creatinine
- Lumbar puncture to exclude meningitis or cover with appropriate antibiotics.

- The diagnosis of severe malaria is based on clinical features and confirmed with laboratory testing. While confirmation of the diagnosis is necessary treatment must be started promptly and not withheld while confirming the diagnosis

TREATMENT OF SEVERE AND COMPLICATED *P. FALCIPARUM* MALARIA

- Patients with severe and complicated malaria preferably are immediately referred to hospitals for admission and in-patient management. If cases referral is not possible, treatment should be started promptly:

TREATMENT

OBJECTIVES

- Administer drugs parenterally to ensure adequate blood-serum concentrations of the drug and rapid clearance of parasitemia
- Provide urgent treatment for life threatening problems e.g., convulsions, hypoglycemia, dehydration, renal impairment
- Prevent death from malaria

Non-pharmacologic

- Clear and maintain the airway.
- Position semi-prone or on side.
- Weigh the patient and calculate dosage.
- Make rapid clinical assessment.
    - Exclude or treat hypoglycemia (more so in pregnant women).
    - Assess state of hydration.
- Measure and monitor urine output.
    - If necessary, insert urethral catheter.
    - Measure urine specific gravity.
- Open IV line for 8 hours of intravenous fluids including diluents for anti-malarial drug, glucose therapy and blood transfusion.

- If rectal temperature exceeds 39°C, remove patient's clothes, use tepid sponge,
- Consider other infections.
- Consider need for anti-convulsant treatment

PHARMACOLOGIC

First line

- **Artesunate**: Weight is < 20kg is 3mg/kg/dose weight >20kg 2.4mg/Kg IV or IM given on admission (time = 0), then repeat at 12 hours, and 24 hours, then once a day for up to 5 days.
- Artesunate is dispensed as a powder of Artesunic acid. From 60mg vials, artesunate must be reconstituted in two steps: initially with sodium bicarbonate solution (Provided), then with 5 ml of 5% glucose (D5W) solution. Full reconstitution results in either 6ml (intravenous concentration 10mg/ml) or 3ml (for intramuscular injection concentration 20mg/ml) of injectable artesunate dosed by weight.

Table 16. 6. Dose regime of Artesunate IV, IM

Weight (kg) (approximate)	IV 10 mg/ml	IM 20 mg/ml
0-8	1 ml	0.5 ml
9 to 12	2 ml	1 ml
13-16	3 ml	1.5 ml
17-18	4 ml	2 ml
19-21	5 ml	2.5 ml
22-25	6 ml	3 ml
26-29*	7 ml	3.5 ml
30-33*	8 ml	4 ml
34-37*	9 ml	4.5 ml
38-41*	10 ml	5 ml
42-46*	11 ml	5.5 ml
47+*	12 ml	6 ml

* For persons weighing more than 25 kg, a second artesunate vial must

be completely reconstituted as above for each dose, and then each dose administered determined by the chart.

Give parenteral antimalarials in the treatment of severe malaria for a minimum of 24 hours, once started (irrespective of the patient's ability to tolerate oral medication earlier)

Alternatives

- **Artemether** IM 3.2 mg/kg loading dose on the first day followed by 1.6 mg/kg daily for two days

  OR

- **Quinine dihydrochloride (IV/IM):** Loading dose: 20 mg/kg in 500 ml of isotonic saline or 5 % dextrose over 4 hours (4ml/minute). The pediatric dose is the same but the fluid replacement must be based on body weight.
- **Maintenance dose**: should be given 12 hours after the start of the loading dose at a dose of 10 mg / kg and it should be given 8 hourly diluted in 500 ml of isotonic saline or 5 % dextrose over 4 hours.

Table 16. 7. Dose regimens of Quinine

Route	Loading dose over 4 hours	Rest for next 8 hours	Maintenance dose over 4 hours (given 12 hours after start of loading Dose)	Rest for 4 hours	Maintainance dose over 4 hours every 8 hourly
IV	20 mg/kg in 10ml/kg D5W over 4 hours (4ml/minute)	Give N/Saline or Ringers lactate to keep vein open and maintain fluid balance	10 mg salt/kg body weight in 500 ml of 5 % dextrose over 4 hours	Give N/Saline or Ringers lactate to keep vein open and maintain fluid balance	10 mg salt/kg body weight in 10ml/kg D5W over 4 hours

	Loading dose	Rest for next 4 hours	Maintainance dose every 8 hourly	
IM	20 mg/kg body weight divided into 2 site (one in each thigh)		10 mg salt/ kg body weight IM into thigh	

- The parenteral treatment should be changed to P.O. only after 24 hours and as soon as the patient's condition improves and if there is no vomiting.
- Oral treatment should be given with Artemether + Lumefantrine in the doses as indicated above. However, if a patient has a history of intake of ***Artemether + Lumefantrine*** before complications developed, give **Quinine** tablets 10 mg salt per kg TID to complete 7 days treatment.

PREVENTION OF MALARIA

- Chemo-prophylaxis

P. Falciparum

First line

- **Mefloquine,** 5 mg base per kg weekly (1tablet for adults >50kg, begin ≥ 2weeks before travel to malariuos area, take weekly on the same day while in the area and for 4 weeks after leaving the area.

Table 16. 8. Dose regimen of Mefloquine as prophylaxis; 5 mg /kg mefloquine (250 mg salt) once weekly

Weight (Kg)	Age (approx.)	Number of tablets per week
<9	< 3 months	5mg/kg salt
9 – 19	3 – 23 months	¼ tablet
20 – 30	2 – 7 year	½
31 – 45	8 – 10 year	¾
36 – 50+	11 – 14+	1

Alternatives

- **Doxycycline,** 100mg daily for adults; 2.2mg/kg daily for children >8yrs; begin 1-2 days before travel to malarious areas, to be taken daily while at the area and after 4 weeks after leaving the area

FURTHER READING

1. Taffese HS, Hemming-Schroeder E, Koepfli C, Tesfaye G, Lee MC, Kazura J, Yan GY, Zhou GF. Malaria epidemiology and interventions in Ethiopia from 2001 to 2016. Infectious diseases of poverty. 2018 Dec; 7(1): 1-9.
2. National malaria guideline 4th ed, 2017

16.2.15 TUBERCULOSIS CHILDREN

BRIEF DESCRIPTION

- Tuberculosis (TB) is a chronic infectious disease caused in most cases by Mycobacterium tuberculosis complex.
- TB may present at any age in children though the risk is highest below the age of 2 years. When compared to adults, children are more prone to TB infection, TB disease, and severe forms of TB disease.
- Diagnosis of TB in children is difficult because of the presence of a wide range of non-specific symptoms.
- It is important to make a clear distinction between infection and disease.
- In infection, only the Mantoux test may be positive (10mm), but the child is healthy and does not have any signs and does not, therefore, need anti TB treatment.
- If there is TB- disease there are clear signs and symptoms.

CAUSES

- Mycobacterium tuberculosis complex (e.g., M. tuberculosis, M. bovis, M. africanum and M. Microti)
- Transmission by droplet inhalation (cough from a patient with open

pulmonary TB); can also be through drinking unpasteurized milk, especially M.bovis

RISK FACTORS

- Contact with infectious (pulmonary) case of TB
- Age < 5 years
- Immunosuppression (HIV, malnutrition, diabetes, etc.).
- Age < 1 year and lack of BCG vaccination are risk factors for severe disease

CLINICAL FEATURES

General symptoms

- Symptoms and signs may be confusing in children co-infected with HIV
- Fever especially in the evening, excessive night sweats
- Recent weight loss and/or failure to gain weight
- Loss of appetite

Pulmonary TB

- Cough lasting for more than 2 weeks (sputum production uncommon in infants and young children
- Dyspnea
- Chest pain, purulent sputum occasionally blood-stained,
- Rales, wheezing and decreased air entry, more common in infants

Extra-pulmonary T B

- It is more common in infants and young children
- Lymph node TB: Localized enlargement of lymph nodes depending on the site affected (commonly neck) Pleural or pericardial effusion
- Abdominal TB: ascites and abdominal pain

- TB meningitis: subacute meningitis (headache, alteration of consciousness)
- Bone or joint TB: swelling and deformity
- Pleural effusion
- TB pericarditis, TB meningitis,
- Bone TB: can be TB spine with gibbus, TB joints with deformity

Complications

- Massive hemoptysis - coughing up >250 mL blood per episode
- Spontaneous pneumothorax and
- Respiratory failure

Diagnosis

- Suspect TB in all children with
    - Fever > 2 weeks
    - Cough >2 weeks (in HIV settings cough of any duration)
    - Poor weight gain for one month
    - Close contact of pulmonary TB case

Investigations

- Chest X-ray: Hilar or mediastinal adenopathy, segmental/lobar infiltrates, military disease, consolidations, pleural effusion, or normal in about 15% of patients
- GeneXpert MTB/Rif: automated DNA test on body samples (sputum, lymphonodes tissue, pleural fluid, CSF etc.), which can diagnose pulmonary TB and determine susceptibility to Rifampicin. It is superior to microscopy.
- GeneXpert MTB/Rif should be used as initial test for TB diagnosis among all presumptive TB patients.
- In facilities with no GeneXpert machines on site, sputum or gastric aspirate or using sputum induction kits for acid-fast stain (ZN stain)

- Other investigations that can be used for sputum and geneXpert negative patients or in case of extra pulmonary TB according to clinical judgment (Chest and spine X ray, abdominal ultrasound, ESR, WBC and differential count, biopsies etc.)
- Sputum culture and Drug susceptibility test: is a confirmatory test for TB and also provides resistance pattern to TB medicines.
- Do this test for:
  - Patients with Rifampicin resistance reported with GeneXpert
  - Also, patients on first-line treatment who remain positive at 3 months and are reported Rifampicin sensitive on GeneXpert
  - Patients suspected to be failing on first-line treatment

Note:

- All presumed and diagnosed TB patients should be offered an HIV test. Bacteriological confirmation of TB is more difficult in children. The diagnosis of TB in children is dependent on conducting a detailed clinical assessment combined with available tests
- Whenever possible, GeneXpert should be performed
- TST is a good supportive test for TB diagnosis in children

DIFFERENTIAL DIAGNOSIS

- Histoplasma pneumonia, trypanosomiasis, brucellosis
- HIV/AIDS
- Malignancy
- Asthma, bronchiectasis, emphysema etc.
- Fungal infection of the lungs e.g., Aspergillosis

Any child:

- Not regaining normal health after measles or whooping cough
- With loss of weight, cough and wheeze not responding to antibiotic

therapy for respiratory disease

- With painless swelling of superficial lymph nodes

TREATMENT

OBJECTIVES

- Avoid complications and mortality
- Cure the infection
- Ensure adequate growth and development

Non-pharmacologic

- Nutritional support
- Emotional support for the child and family
- Prevention of peripheral neuropathy

PHARMACOLOGIC

- Treatment of TB in children is similar with that of adults with a combination of 4 or more anti-TB drugs. The treatment is standardized by putting patients into different treatment groups based on smear status and previous history of treatment for TB. TB treatment strategy is referred to as DOT indicating that treatment is given under direct observation of a health worker or treatment supporter daily throughout the course of treatment.

TREATMENT WITH 1ST LINE ANTI-TB DRUGS

- TB Patients with strains susceptible to first line anti-TB drugs are treated with standardized first line treatment regimen either for 6 months.
- First line anti-TB drugs available for TB treatment in Ethiopia:
  - Rifampicin(R); Ethambutol (E); Isoniazid (H); Pyrazinamide (Z)

The fixed dose combination (FDC) and loose drugs available for children are:

- RHZ (60,30,150); RH (60,30); RH (60,60); E (100); INH (100)

Table 16. 9. Recommended Doses of First-Line Anti-tuberculosis Drugs

Drugs	**Recommended dose**	
	Dose and range(mg/kg)	**Maximum**(mg)
Isoniazid (H)	5 (4–6)	300
Rifampicin (R)	10 (8–12)	600
Pyrazinamide (Z)	25 (20–30)	2,000
Ethambutol (E)	15 (15–20)	1600

Table 16. 10. FDC dosing regimens for paediatric new cases

Weight (kg)	Intensive phase (2 months)			Continuation phase (4 months)		
	RHZ (60,30,150)	RHZE (150,75,400,275)	E (100)	RH (150,75)	RH (60,30)	RH (60,60)
5 to 7	1		1		1	1
8 to 14	2		2		2	1
15 to 20	3		3		3	2

Table 16. 11. FDC dose regimens for Retreatment Cases for children

Weight (kg)	Intensive phase (3Months)			Continuation phase (5Months)				
	RHZ (60,30, 150)	RHZE (150,75, 400, 275)	E (100)	RH (60,30)	RH (150,75)	RH (60,60)	E (100)	E (400)
5 to 7	1		1	1		1	1	
8 to 14	2		2	2		1	2	
15 to 20	3		3	3		2	3	
21 to 30*		2			2	2		1

Further reading

1. Seid MA, Ayalew MB, Muche EA, Gebreyohannes EA, Abegaz TM. Drug-susceptible tuberculosis treatment success and associated factors in Ethiopia from 2005 to 2017: a systematic review and meta-analysis. BMJ open. 2018 Sep 1;8(9):e022111.
2. Nation guideline for TB, DR Tb and leprosy in Ethiopia, 2017

16.2.16 HIV/AIDS IN CHILDREN

BRIEF DESCRIPTION

- HIV/AIDS has created an enormous challenge to mankind since its recognition; close to 65 million people are infected and about 36 million people are living with HIV, out of which about 2.6 million are children under 15 years of age. Of these children, 90% live in sub-Saharan Africa live.
- Mother-to-child transmission is the primary mode of HIV acquisition in children accounting for about 90% of cases; therefore, the most efficient and cost-effective way to tackle pediatric HIV globally is to reduce mother-to-child transmission (MTCT).
- ART has radically changed the natural course of HIV infection in countries where it has been successfully implemented and HIV-infected infants and children now survive to adolescence and adulthood.
- As part of its continued efforts to prevent further spread of HIV and to improve the quality of HIV care and treatment service, the government of Ethiopia is:
    - Adopting and introducing new antiretroviral medicines (ARVs) with proven safety and efficacy. Accordingly, Dolutegravir (DTG) is one of those ARVs included into the 2018 edition of the national comprehensive HIV prevention, care and treatment guidelines of Ethiopia.
    - Working to optimize pediatric ART by introducing preferred and optimal ARVs.
    - Adopting and introducing third line ART service.

CARE OF THE HIV-EXPOSED INFANT

- HIV-exposed infants need regular follow-up since it is difficult to exclude HIV infection at early age and as they are at higher risk of morbidity and mortality regardless of infection status.
- Goals of Care for the HIV-Exposed Infants are to:
  - Recognize HIV infection early using age-appropriate testing
  - Enroll early HIV-infected children into ART care
  - Minimize risk of vertical transmission of HIV

COMPREHENSIVE CARE FOR THE HIV-EXPOSED INFANT (HEI)

- Infants should be seen monthly for the first six months and then every three months.
- Infants with poor growth, failure to thrive, or recurrent illnesses should have more frequent close follow-up.
- Care for HIV exposed infants should start at birth.
- Mothers should be given appointment for the first postnatal visit at delivery.
- Mothers who do not deliver at a health facility should be given appointment at first contact.
- With the healthcare system.
- Mothers should be counseled on infant prophylaxis
- Immunizations should be given according to the National Expanded Program on Immunization
- Counseling on infant feeding, maternal nutrition and support
- Follow-up Visit at 6 weeks of age
- Components of HEI care at this visit include:
- History: Including use of PMTCT, parental concerns, inter-current illnesses.

- Nutrition and growth assessment- plot weight, height and head circumference on the growth chart
- Developmental assessment using developmental check list provided
- TB risk assessment: Screen for TB disease by using TB screening tool
- Physical examination: Giving special emphasis for symptoms and signs suggestive of HIV infection.
- Determination of HIV status: All HIV exposed infants should have the initial DNA PCR test done at six weeks of age
- Caregivers should be counseled on the rationale for infant diagnosis; explain the possible test results, and need for additional testing to determine infection status definitely.
- Cotrimoxazole preventive therapy should be provided to all HIV- exposed infants starting at six weeks of age, and continued until HIV infection has been excluded and infant is no longer at risk from breastfeeding
- Infant for ARV prophylaxis: Ensure that ARV provision to the infant is per the national guideline for PMTCT
- Follow-up visit for HIV-exposed infants at two months:
- Infants should be assessed to ensure they are tolerating Cotrimoxazole.
- Results of the initial DNA PCR test should be made available to care giver.
- In every visit the above assessments should be done including inter-current illness evaluation.

ANTIRETROVIRAL THERAPY IN CHILDREN

Table 16. 12. Updated summary of first-line ART regimens

Population	Preferred first-line regimens	Alternative first-line regimens	Special circumstances
Adolescents (10 to 19 years OR weight ≥30 kg) (*Including those with TB/HIV co infection.*)	TDF+3TC+DTG (FDC)	TDF+3TC+EFV AZT + 3TC + EFV ABC + 3TC + EFV	TDF+3TC + ATV/r AZT+3TC + ATV/r
Children less than 10 years or weight. ≥ 20kg)	ABC + 3TC + DTG	ABC+ 3TC+EFV AZT+3TC+DTG AZT+3TC+EFV ABC+ 3TC+LPV/r	ABC+3TC+NVP AZT+3TC+NVP
Children between 4 weeks and 10 years and body weight <20yrs	ABC+3TC+LPV/r	No alternative first line regimen for this group.	ABC+3TC+EFV AZT + 3TC +EFV (or NVP) AZT + 3TC +LPV/r

REFERENCE

1. http://www.aids.gov/hiv-aids-basics/hiv-aids-101global-statistics.
2. National HIV treatment guidelines of Ethiopia, 2018

COMMON OPPORTUNISTIC INFECTIONS/CONDITIONS IN CHILDREN WITH HIV/AIDS

ORAL THRUSH

BRIEF DESCRIPTION

- This is a condition caused by candida species and is a punctate or diffuse erythema and white pseudomembranous plaque affecting the oral mucosa.
- The lesions may become confluent plagues involving extensive regions of the mucosa. Plaques can be removed with difficulty to reveal a granular base that bleeds easily.
- After the neonatal period, the presence of oral thrush-without antibiotic treatment, or lasting over 30 days despite treatment or recurring is highly suggestive HIV infection.

CLINICAL FEATURES

- Pain and difficulty of feeding
- Fever, occasional
- Vomiting if extends to the esophagus
- Whitish curd-like plaques on the tongue and oral mucosa
- Bleeding upon removal of the plaque
- Evidence for immunosuppression usually present, especially beyond the neonatal period

Investigations

- Diagnosis of oral thrush is entirely clinical and investigations are not needed

Treatment

Objectives

- Alleviate symptoms and improve feeding

- Decrease the risk of complications
- Identify the underlying cause, if any

Non-pharmacologic

- Support feeding (if admitted, use naso-gastric tube feeding, especially in severe cases)

PHARMACOLOGIC

First line

- **Nystatin** (100 000 units/ml) suspension: Give 1-2ml into the mouth 4 times a day for 7 days.

Alternatives

- **Miconazole oral gel**, apply thin films of 2% cream BID for four days or until lesion disappears
- Systemic anti-fungal like fluconazole is needed if there is no improvement or extension to esophagus.

PNEUMOCYSTIS PNEUMONIA (PCP)

Brief description

- A presumptive diagnosis of pneumocystis pneumonia can be made in a child who has severe or very severe pneumonia and bilateral interstitial infiltrate on chest x-ray.
- Consider the possibility of pneumocystis carinii pneumonia in children, known or suspected to have HIV, whose ordinary pneumonia does not respond to treatment.
- Pneumocystis pneumonia occurs most frequently in infants (especially those <6 months of age).
- Interstitial pneumonitis caused by the parasite Pneumocystis jirovecii (formerly carinii).
- It is common in severely immunosuppressed patients (e.g., in HIV).

CLINICAL FEATURES

- Fever, dry cough, fast breathing, flaring, cyanosis, dyspnea, intercostal and subcostal retractions, crackles and rhonchi on chest examination
- In children highest incidence is seen between 2-6 months of age and is characterized by abrupt onset of fever, tachypnea, dyspnea and cyanosis.

INVESTIGATIONS

- Diagnosis is based on high index of suspicion from clinical features and presence of an underlying immunosuppression
- Chest X-ray may be normal in early disease, but may show diffuse bilateral infiltrates extending from the perihilar region are visible in most patient
- Pulse oximetry
- Serum LDH levels, usually elevated and decrease with successful treatment

TREATMENT

OBJECTIVES

- Prevent respiratory failure
- Decrease the risk of complications
- Shorten hospital stay

Non-pharmacologic

- Oxygen via facemask or nasal cannula
- Appropriate fluid management

PHARMACOLOGIC

First line

- **Cotrimoxazole,** Trimetoprime component 15-25mg/kg/day in 3-4 divided doses a day for 3 weeks.

Alternative

- **Pentamidine** (4mg/kg once per day) by IV infusion for 3 weeks

  - ADRs: Renal impairment, pancreatitis, leucopenia, hypoglycemia
  - C/Is: Diabetes, renal damage
- Alternative regimen (21-day course) if above not available/ tolerated: Clindamycin mg every 8 hours Plus dapsone 100 mg daily
- Prednisolone 2mg/kg per day for the first 7 - 10 days followed by a tapering regimen for the next 10 - 14 days.

PROPHYLAXIS

- **Trimethoprim,** 5mg/kg/24 hours and Sulfamethoxazole 25mg/kg/24 hours orally divided Q12 hours OR Q24 hours 3 days /week on consecutive days. OR Q12 hours 7 days a week OR Q12 hours on alternative days 3days /week

Note: Children who have had PCP should receive lifelong prophylaxis

Reference

- Saltzman RW, Albin S, Russo P, Sullivan KE. Clinical conditions associated with PCP in children. Pediatric pulmonology. 2012 May;47(5):510-6.
- Patil S, Rao RS, Majumdar B, Anil S. Clinical appearance of oral Candida infection and therapeutic strategies. Frontiers in microbiology. 2015 Dec 17; 6:1391.
- National guideline comprehensive HIV prevention, care and treatment guideline, 2018

16.3 RESPIRATORY AND AIRWAY DISEASES IN CHILDREN

16.3.1 BRONCHIAL ASTHMA

BRIEF DESCRIPTION

- Bronchial asthma is a disease characterized by recurrent, reversible airway obstruction, airway inflammation and increased airway responsiveness to a variety of stimuli (hyper- reactive airway).

- Symptoms are usually triggered or aggravated by viral infection of the respiratory tract or inhaled allergens.

CAUSES

- Not known but associated with allergies, inherited and environmental factors

CLINICAL FEATURE

- Cough - usually dry, may be intermittent, persistent, or acute, especially at night
- No fever (if fever present, refer to pneumonia)
- Difficulty in breathing (usually recurrent attacks) with chest tightness, with or without use of accessory muscles -reported by older children.
- Patients may not appear very distressed despite a severe attack
- Wheezing, rhonchi: recurrent wheezing (mostly expiratory) which is severe at night
- Severe forms: failure to complete sentences, darkening of lips, oral mucosa and extremities (cyanosis)

FINDING ON EXAMINATION

- Tachypnea, hyper-inflation of the chest, lower chest wall in drawing
- Prolonged expiration with audible wheeze
- Reduced air intake when obstruction is severe absence of fever
- Good response to treatment with a bronchodilator.

Danger signs during acute attacks:

- Paradoxical breathing
- Profound diaphoresis
- Cyanosis
- Silent chest on auscultation
- Drowsiness or confusion
- Agitation
- Exhaustion
- Arrhythmia

DIFFERENTIAL DIAGNOSIS

- Heart failure
- Other causes of chronic cough
- Bronchiolitis
- Bronchiectasis

INVESTIGATIONS

- Diagnosis of childhood asthma is generally made on clinical grounds and investigations are not needed unless complication or concurrent chest infection is suspected.

SPECIALIZED INVESTIGATIONS

- Peak flow rate: the peak flow rate increases to about 200 ml following administration of a bronchodilator
- Sputum: for eosinophilia

IF EVIDENCE OF BACTERIAL INFECTION

- Chest X-ray: if complications like pneumothorax, atelectasis or concurrent pneumonia is suspected, CBC

ASTHMA, ACUTE EXACERBATION

Mild or moderate

- Talks in phrases, prefers sitting to lying, Not agitated
- Respiratory rate increased; Accessory muscles not used
- Pulse rate (beats per minute)
- Child >5 years: <125bpm
- Child <5 years: 140bpm
- Oxygen saturation in air > 92%
- PEF >50% predicted or best

Severe

- Talks in words or Cannot complete sentences in one breath or, too breathless to talk or feed
- Sits hunched forward, Agitated, Drowsy, Confused
- Respiratory rate > 30/min
- Use of accessory muscles for breathing (young children)
- Respiratory rate
  - Child > 5 years: > 30
  - Child < 5 years: >40
- Pulse (beats/minute)
  - Child > 5 years: > 125 bpm
  - Child <5 years: > 140 bpm
- PEF < 50% predicted or best Life threatening
- SpO2 < 92%

Life threatening/impending RF

- Silent chest, feeble respiratory effort, cyanosis
- Hypotension, bradycardia or exhaustion, agitation
- Reduced level of consciousness
- Peak flow < 33% of predicted or best
- Arterial oxygen saturation < 92%

Treatment

Objective

- Relieve symptoms
- Prevent respiratory failure

General principles of management

- Inhalation route is always preferred as it delivers the medicines directly to the airways; the dose required is smaller, the side-effects are reduced
- E.g., nebulizer solutions for acute severe asthma are given over 5-10 minutes, usually driven by oxygen in hospital
- In children having acute attacks, use spacers to administer inhaler puffs
- Oral route may be used if inhalation is not possible but systemic side-effects occur more frequently, onset of action is slower and dose required is higher
- Parenteral route is used only in very severe cases when nebulization is not adequate

ACUTE ASTHMATIC ATTACK IN CHILDREN

MILD TO MODERATE

Non-pharmacologic

- Treat as an out-patient
- Reassure patient; place him in a. sitting position

Pharmacologic

- Give salbutamol Inhaler 6 puffs for children < 6 years, 12puffs for those >6 years.
  - Spacer can be prepared from locally available materials like plastic water bottles (volume 100-600ml
  - After giving salbutamol with rapid succession, one should wait until the patient breaths 3-5 times before putting off the spacer.
  - Or 5 mg (2.5 mg in children) nebulization
  - Repeat every 20-30 min if necessary
- Steroid is only for moderate attacks.
  - Prednisolone 50 mg (1 mg/kg for children)
  - IV hydrocortisone 4-5mg/kg Q6hrs
- Monitor response for 30-60 min.
  - If not improving or relapse in 3-4 hour -Refer to higher level
- If improving, send home with
  - 2-6 puff salbutamol Q4-6 hours as needed
  - Prednisolone 1 mg/kg once a day for 3 days for children
  - Instruct the patients on self-treatment and when to come back
  - Review in 48 hours
  - Do not give routine antibiotics unless there are clear signs of bacterial infection

SEVERE ASTHMA

NON-PHARMACOLOGIC

- Admit, Positioning: upright or leaning position in older children.
- Oxygen: administer oxygen via mask or nasal prongs/cannula. Continue oxygen therapy until the signs of hypoxia are no longer present or maintain the SpO2>94%

- Treatment of comorbid conditions: rhinitis, sinusitis or pneumonia as appropriate.
- Nutrition: Increase feeding and fluid intake as appropriate.

PHARMACOLOGIC

First-line

MANAGEMENT OF SEVERE ACUTE ASTHMA

- Put on intranasal oxygen 2-4 liters/minute
- Start salbutamol 6 puff for children <6 years, 12 puffs for children >6 years every 20 minutes
- Hydrocortisone 4-5mg/kg/dose every 6 hours. Start steroid together with salbutamol.
- Epinephrine challenge:
    - Can be considered if the patient has silent chest or any other sign of impending respiratory failure, and when salbutamol puff or nebulized is not available.
    - Dose: epinephrine 1 in 1000 preparation 0.01ml/kg (maximum 0.3ml (if diluted to 1/10,000 (by adding 1 ampoule of epinephrine to 9ml of normal saline), the dose is 0.1ml/kg (max 3ml).
    - Can be repeated once if no improvement after 15 minutes.
- If the above measures fail, magnesium sulphate 50% solution at a dose of 0.1ml/kg/ dose can be given. Dilute to 20% to give IM and to 10% solution to give IV (give over 20 minutes).
- Aminophylline is reserved for case unresponsive for the above measures.
    - Dose: loading dose 5-6mg/kg, the maintenance dose of 3-5mg/kg/dose IV every 6 hours.
    - Administration: diluted in D5W to be given over 1 hour.
    - Discontinue or omit subsequent doses if the child develops vomiting, tachycardia >180beats per minute, or convulsion

Follow-up

- Review within 24 hours
- Monitor symptoms and peak flow
- Arrange self-management plan

Asthma, long-term management

General principles of management

- Follow a stepped approach
- Before initiating a new drug, check that diagnosis is correct, compliance and inhaler technique are correct and eliminate trigger factors for acute exacerbations
- Start at the step most appropriate to initial severity
- Rescue course
- Beclomethasone inhaler is preferred than systemic steroid in current guideline
- Mouth gargling after use to decrease risk of oral thrush Or Give a 3-5 days "rescue course" of prednisolone at any step and at any time as required to control acute exacerbations of asthma at a dose of prednisone: Child < 1 year: 1-2 mg/kg daily; 1-5 years: up to 20 mg daily; 5-15 years: Up to 40 mg daily; adult: 40-60 mg daily for up to 3-5 days.
- Stepping down
- Review treatment every 3-6 months
- If control is achieved, stepwise reduction may be possible
- If treatment started recently at Step 4 (or contained corticosteroid tablets, see below), reduction may take place after a short interval; in other patients 1-3 months or longer of stability may be needed before stepwise reduction can be done

TREATMENT

STEP 1: Intermittent asthma

- Intermittent symptoms (< once/week)
- Night time symptoms < twice/month
- Normal physical activity

Occasional relief bronchodilator

- Inhaled short-acting beta2 agonist e.g., salbutamol inhaler 2 puffs
- **Dosage form:** Metered Dose Inhaler or MDI 100mcg/puff
- Move to Step 2 if use of salbutamol needed more than twice a week or if there are night-time symptoms at least once a week

STEP 2: Mild persistent asthma

- Symptoms > once/week, but < once/day
- Night time symptoms > twice/month
- Symptoms may affect activity

Regular inhaled preventer therapy

- Salbutamol inhaler 1-2 puffs prn
- PLUS, regular standard-dose inhaled corticosteroid, e.g., beclomethasone: 40-80mcg every 12 hours)
- Assess after 1 month and adjust the dose prn
- Higher dose may be needed initially to gain control
- Doubling of the regular dose may be useful to cover exacerbations

STEP 3: Moderate persistent asthma

- Daily symptoms
- Symptoms affect activity
- Night time symptoms > once/week

Daily use of salbutamol

- Children below 5 years: refer to specialist
- Regular high-dose inhaled corticosteroids
- Salbutamol inhaler 1-2 puffs prn up to 2-3 hourly Usually 4-12 hourly
- PLUS, beclomethasone inhaler in child 5-12 years: 100-400 micrograms every 12 hours)

STEP 4: Severe persistent asthma

- Daily symptoms
- Frequent night time symptoms

Daily use of salbutamol

- Refer to specialist clinic especially children <12 years
- Salbutamol (as in Step 3) plus
- Regular high-dose beclomethasone (as in Step 3) Plus regular prednisolone 10-20 mg daily after
- Breakfast

Note

- If inhaler not available, consider salbutamol tablets/syrup
    - Child < 2 years: 100 micrograms/kg per dose
    - Child 2-5 years: 1-2 mg per dose

Caution

- Do not give medicines such as morphine, propranolol, or other B-blockers to patients with asthma as they worsen respiratory problems
- Do not give sedatives to children with asthma, even if they are restless

Prevention

- Avoid precipitating factors e.g.

  - Known allergens such as dust, pollens, animal skins
  - Exposure to cold air
  - Exercise can precipitate asthma in children, advise them to keep an inhaler handy during sports and play
  - Effectively treat respiratory infections

FURTHER READING

1. Woldetsadik MD, Kumie A. PREVALENCE OF SYMPTOMS OF ASTHMA AND ASSOCIATED FACTORS AMONG PRIMARY SCHOOL CHILDREN IN ADDIS ABABA. Ethiopian Medical Journal. 2018 Sep 30;56(4).
2. Jain A, Bhat HV, Acharya D. Prevalence of bronchial asthma in rural Indian children: A cross sectional study from South India. The Indian Journal of Pediatrics. 2010 Jan 1;77(1):31-5.

16.3.2 BRONCHIOLITIS

Brief description

- Acute inflammatory obstructive disease of small airways (bronchioles) common in children less than 2 years.

Causes

- Mainly viral (often respiratory syncytial virus, RSV)

Clinical features

- First 24-72 hours: rhinopharyngitis with dry cough
- Later tachypnoea, difficulty in breathing, wheezing (poorly responsive to bronchodilators)
- Cough (profuse, frothy, obstructive secretions)
- Mucoid nasal discharge
- Moderate or no fever

- Criteria for severity: child < 3 months, worsening of general condition, pallor, cyanosis, respiratory distress, anxiety, respiratory rate >60/minute, difficulty feeding, SpO2 < 92%

Differential diagnosis

- Asthma
- Pneumonia, whooping cough
- Foreign body inhalation
- Heart failure

Investigations

- Mainly Clinical diagnosis
- X-ray: Chest (to exclude pneumonia)

Treatment

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Mild-moderate bronchiolitis (Wheezing, 50-60 breaths/minute, no cyanosis, able to drink/feed)
    - ○ Treat the symptoms (possibly as an out-patient)
    - ○ Nasal irrigation with normal saline
    - ○ Small, frequent feeds
    - ○ Increased fluids and nutrition

Severe bronchiolitis (Wheezing, fast breathing > 60 breaths/min, cyanosis)

- ○ Admit and give supportive treatment as above
- ○ Give humidified nasal-oxygen (1-2 liters/min)

  - Give basic total fluid requirement of 150 ml/kg in 24 hours plus extra to cover increased losses due to illness

Pharmacologic

- Treat fever (paracetamol)
- Salbutamol inhaler 100 micrograms/puff: 2 puffs with spacer, every 30 minutes or nebulization salbutamol 2.5 mg in 4 ml normal saline.
- If symptoms improve, continue salbutamol every 6 hours
- If symptoms non-responsive, stop the salbutamol
- Nebulize Adrenaline 1:1000, 1 ml diluted in 2-4 ml normal saline every 2-4 hours
- Give as much oral fluids as the child will take: e.g. ORS. Use NGT or IV line if child cannot take orally
- Antibiotics for suspected superimposed infection

FURTHER READING

1. Meissner HC. Viral bronchiolitis in children. New England Journal of Medicine. 2016 Jan 7;374(1):62-72.
2. Spurling GK, Doust J, Del Mar CB, Eriksson L. Antibiotics for bronchiolitis in children. Cochrane Database of systematic reviews. 2011(6).

16.3.3 CROUP (ACUTE LARYNGO-TRACHEO-BRONCHITIS)

BRIEF DESCRIPTION

- Infectious croup is a syndrome caused by upper airway obstruction due to infection of the larynx and trachea.
- The term croup has been used to describe a variety of upper respiratory conditions in children, including laryngitis, laryngotracheitis, laryngotracheobronchitis, bacterial tracheitis, or spasmodic croup.

- Infants and young children develop more severe disease because of their narrow upper airway.

CLINICAL FEATURES

- Inspiratory stridor, hoarseness of voice, brassy (barking) cough, apnea
- Symptoms and signs of upper respiratory tract infection
- May have fever, but no sign of toxicity

Danger signs

- Severe stridor on inspiration and expiration
- None or markedly reduced air entry
- Change in sensorium (lethargic or unconscious)
- Duskiness or cyanosis

Table 16. 13. Modified Westley Clinical Scoring System for Croup

	0	1	2	3	4	5
Inspiratory Stridor	Not present	When agitated/ active	At rest			
Intercostal recession		Mild	Moderate	Severe		
Air entry	Normal	Mild decreased	Severely decreased			
Cyanosis	None				With agitation/ activity	At rest
Level of consciousness	Normal					Altered
Total possible Score = 0 – 17. *4= Mild Croup; 4 – 6= Moderate Croup; >6= Severe Croup*						

INVESTIGATIONS

- The diagnosis of croup is generally clinical and investigations are seldom required.
- Neck X-ray: Sub-glottic narrowing of the trachea ("pencil end") appearance.
- Chest X-ray: If complications or comorbid chest infections are suspected.

TREATMENT

Objectives

- Prevent respiratory failure
- Relieve symptoms

Non-pharmacologic

- Children with croup need minimal handling. This includes limiting examination, nursing with parents.
- Supplemental oxygen is not usually required. If needed, consider severe airways obstruction.
- Do not forcibly change a child's posture - they will adopt the posture that minimizes airways obstruction.
- Iv access should be deferred.
- Avoid distressing the child further.

PHARMACOLOGIC

Mild to Moderate Croup

- **Prednisolone** 1mg/kg,AND prescribe a second dose for the next evening.
  OR
- A single dose of **Oral Dexamethasone** 0.15mg/kg if available.
- Observe for half an hour post steroid administration.
- Discharge once stridor-free at rest.

Severe Croup

- **Dexamethasone**, 0.6mg/kg IM, single dose (for severe cases).

Additional

- **L-epinephrine (nebulized),** 0.5ml/kg of 1:1000 (1mg/ml) in 3ml NS (maximum dose is 2.5ml for age ≤4years old, 5ml for age >4years old).
- **Racemic epinephrine:** 0.05ml/kg diluted in 3ml total volume normal saline
- Hospitalize the child if more than one nebulization is required

REFERENCE:

1. Bjornson C, Russell KF, Vandermeer B, Durec T, Klassen TP, Johnson DW. Nebulized epinephrine for croup in children. Cochrane database of systematic reviews. 2011(2).
2. Westley CR, Cotton EK, Brooks JG; Nebulized racemic epinephrine by IPPB for the treatment of croup: a double-blind study; Am J Dis Child. 1978 May; 132(5):484-7.

16.3.4 EPIGLOTTITIS

ACUTE EPIGLOTTITIS

BRIEF DESCRIPTION

- Epiglottitis is an acute inflammation of the epiglottis.
- It is rare diseases of young children since routine childhood immunization with Hib vaccine was introduced.
- Airway obstruction is always severe, and intubation or tracheostomy is often needed.

CAUSE

- Bacterial infection, commonly Haemophiles influenzae type b

CLINICAL FEATURES

- Rapid onset of high fever

- Typical: "tripod or sniffing" position, preferring to sit, leaning forward with an open mouth, appears anxious
    - Sore throat, difficulty swallowing, drooling, respiratory distress
    - Stridor and may be cough
    - Appears critically ill (weak, grunting, crying, drowsy, does smile, anxious gaze, pallor, cyanosis)
    - Asphyxia leading to quick death

Differential diagnosis

- Laryngeal cause of stridor e.g., laryngotracheobronchitis

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Admit and treat as an emergency – intubation or tracheostomy may often be needed
- Insert IV line and provide IV hydration

PHARMACOLOGIC

- Ceftriaxone 50 mg/kg once daily for 7-10 days

PREVENTION

- Hib vaccine is part of the pentavalent DPT/HepB/Hib vaccine used in routine immunization of children

FURTHER READING

1. Adair JC, RING WH. Management of epiglottitis in children. Anesthesia & Analgesia. 1975 Sep 1;54(5):622-5.
2. World Health Organization, World Health Organization. Department of Child, Adolescent Health, UNICEF.

16.4 RENAL AND UROLOGIC DISEASES IN CHILDREN

16.4 .1 ACUTE GLOMERULONEPHRITIS

BRIEF DESCRIPTION

- Acute post streptococcal glomerulonephritis is one of the non-suppurative complications of streptococcal leading to acute inflammation of renal glomeruli (small blood vessels in the kidney).

CAUSE

- An immune reaction often follows streptococcal throat infection by a latent period of 1-2 weeks and skin infection by 4–6 weeks.
- The condition is characterized by a sudden onset of hematuria, oliguria, edema and hypertension.
- Common in children >3 years and adolescents

CLINICAL FEATURES

- Hematuria (usually described as smoky or cola colored)
- Edema (usually periorbital and pretibial, but may be generalized)
- Discomfort in the kidney area (abdominal or back pain), Anorexia, General weakness (malaise)
- Hypertension (may complicate to hypertensive encephalopathy or Heart Failure)
- Decreased urine output
- Evidence of primary streptococcal infection:
  - Usually as acute tonsillitis with cervical adenitis
  - Less often as skin sepsis

INVESTIGATIONS

- Urinalysis: Macroscopic or microscopic hematuria (RBC>5/hpf), RBC casts, WBC, cellular casts
- Proteinuria: Rarely exceeding 3+
- Blood chemistry: BUN, Creatinine, sodium, potassium levels
- EKG for evidence of hyperkalemia
- ESR or C-reactive protein
- Complete Blood Count, ASO titer
- Renal ultrasound (not essential to diagnosis)

TREATMENT

Objectives

- Avoid complications of hypertension and hyperkalemia
- Relieve edema
- Treat renal failure

Non-pharmacologic

- Input and output monitoring chart and daily weight measurements
- Salt restriction and regulate protein
- Restrict fluid input: determine 24-hour fluid requirement (400ml/m2/24hours + urine output+ any other losses)
- Giving maintenance fluid orally unless there is indication to give intravenously

PHARMACOLOGIC

- Treat any continuing hypertension
- Treat primary streptococcal infection (10-day course): Amoxicillin 20 mg/kg per dose every 8 hours for 10 days
- If allergic to penicillin: Erythromycin 15 mg/kg per dose every 6 hours for 10days

- For fluid overload (oedema): Furosemide 1 mg/kg IV (slow bolus) every 6-12 hours
- If furosemide is not enough to control the blood pressure, add nifedipine 0.25-0.5mg/kg/dose Q6hours (maximum dose 10mg/dose or 3mg/kg/24hours).,
- If hyperkalemia (serum potassium > 5.5mmol/liter), give calcium gluconate 10%, 0.5ml/kg IV over 10 minutes, OR Glucose 5-10ml/kg of 10% dextrose over 1 hour and regular insulin 0.1-0.2units/kg as a bolus Refer: for peritoneal dialysis if the above measures fail.

PREVENTION

- Treat throat and skin infections promptly and effectively
- Avoid overcrowding
- Adequate ventilation in dwellings

FURTHER READING

1. Gebreyesus LG, Aregay AF, Gebrekidan KG, Alemayehu YH. Factors associated with treatment outcome of acute post streptococcal glomerulonephritis among patients less than 18 years in Mekelle City, Public Hospitals, North Ethiopia. BMC research notes. 2018 Dec 1;11(1):693.
2. Abdissa A, Asrat D, Kronvall G, Shitu B, Achiko D, Zeidan M, Yamuah LK, Aseffa A. Throat carriage rate and antimicrobial susceptibility pattern of group A Streptococci (GAS) in healthy Ethiopian school children. Ethiop Med J. 2011 Apr;49(2):125-30.

NEPHROTIC SYNDROME

BRIEF DESCRIPTION

- Nephrotic syndrome is characterized by heavy proteinuria (40mg/m2/hour on timed urine collection or spot urine protein to urine Creatinine ratio > 2, or dipstick on early morning urine sample of 3+ or 4+), hypoalbuminemia (<2.5gm/dl), hypercholesterolemia (> 200mg/dl) and edema.

CAUSES/EPIDEMIOLOGY

- About 90% of children beyond one year of age and less than 12 years of age, with nephrotic syndrome have minimal change disease with steroid responsiveness.
- The commonest age at presentation is 2 – 6 years.
- After an apparent response to steroid treatment a patient may have relapse, which is defined as proteinuria of 3+ or more on dipstick for 3 consecutive days with or without edema. Other causes are congenital (rare).
- Secondary: Due to post-streptococcal acute glomerulonephritis, malaria, allergy, UTI, hepatitis B, HIV

CLINICAL FEATURES

- Periorbital and pedal edema
- Generalized edema, including ascites and pleural effusion in some patients
- Hypertension: Generally rare but can occur in some patients

INVESTIGATIONS

- Urine dipstick (protein, blood)
- Early morning spot urine protein to creatinine ratio or 24hour urine protein quantification
- Serum albumin, cholesterol, BUN, Creatinine
- Complete blood count

DIFFERENTIAL DIAGNOSIS

- Cardiac failure, liver disease
- Malnutrition with oedema e.g., kwashiorkor
- Malabsorption syndrome
- Allergic states causing generalized body swelling
- Chronic glomerulonephritis

TREATMENT

Objectives

- Relieve symptoms
- Alleviate proteinuria
- Spare the kidney from damage by proteinuria

Non-pharmacologic

- While the child is edematous, restrict salt (2g daily, i.e. less than a half TSP/ day) and reduce maintenance fluid to 70% of normality.
- Critical assessment of temperature, blood pressure, and pulse, capillary refill time and weight changes
- Educate the child and family about the disease, its management and its prognosis.

PHARMACOLOGIC

- **Prednisolone**, 60mg/m2 or 2mg/kg (maximum dose of 80mg) once daily for 6 weeks,
  - Followed by 40mg/m2 (1.5mg/kg) given as a single dose on alternate days for a further 6 weeks after a meal to prevent gastrointestinal upsets.
  - Gradually reduce the dose after the first 4 weeks, e.g., reduce by 0.5 mg/kg per day each week
- When oedema has subsided and if still hypertensive:
  - Give appropriate treatment
  - Furosemide: 1-2 mg/kg per dose each morning to induce diuresis
  - Caution is needed when diuretics are prescribed because of hypovolemia, risk of hypercoagulability
- If clinical signs of/suspected streptococcal infection:
  - Give antibiotic as in Acute glomerulonephritis

- If patient from area of endemic schistosomiasis:
    - Praziquantel 40 mg/kg single dose
- **If no improvement after 4 weeks or patient relapses:**
    - Refer for further management

TREATMENT STEROID RESISTANCE

- If a patient fails to respond to 4 weeks of steroid treatment, then steroid resistance is diagnosed and the patient should be referred for renal biopsy and further treatment.
- If the child is edematous, give empirical **amoxicillin** 50mg/kg in two divided doses till the edema disappears.
- If slightest suspicion of infection, treat with 3rd generation cephalosporins and or **gentamycin** for 7 – 10days

TREATMENT OF RELAPSING DISEASE

- If infrequent relapse (< 2 relapses in 6 months or < 3 relapses in one year),
    - **Prednisolone** 60mg/m2 (maximum 80mg) daily until urinary protein turns negative or trace for 3 consecutive days followed by alternate day therapy with 40mg/m2 (maximum 60mg) for 28 days or 14 doses.
- If frequent relapse (2 or more relapses in the initial 6 months or more than 3 relapses in any 12 months),
    - **Prednisolone** 60mg/m2 (maximum 80mg) daily until urinary protein turns negative or trace for 3 consecutive days followed by alternate day therapy with 0.1-0.5mg/kg for 6 months and then taper.
- If the child relapses while on alternate day prednisolone,
    - add levamisole 2.5mg/kg on alternate days for 6-12 months, then taper prednisolone and continue levamisole for 2-3 years.
- If the child develops steroid toxicity, refer to a tertiary center.
- ACE inhibitors:
- Steroid resistant NS: option of referral

FURTHER READING

1. Mola K, Shimelis D. Pattern and outcome of renal diseases in hospitalized children in Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia. Ethiopian Medical Journal. 2016 Jun 9;54(3)
2. Handbook for the management of common renal disorders in Ethiopia, 2009
3. Pediatric nephrology, 7th ed, 2016

16.4.2 ACUTE KIDNEY INJURY

BRIEF DESCRIPTION

- Acute impairment of renal function.

CAUSES

- Compromised renal perfusion e.g., dehydration, heart failure, shock (acute)
- Obstructed urinary flow
- Damage to renal tissue by infectious and inflammatory diseases (e.g., glomerulonephritis), intoxications, nephrotoxic drugs

CLINICAL FEATURES

- Oliguria (urine flow <1 ml/kg/hour)
- Generalized oedema
- Hypertension, heart failure, dyspnoea
- Nausea and vomiting, anorexia
- Lethargy, convulsions

DIFFERENTIAL DIAGNOSIS

- Other renal disorders
- Biventricular heart failure

INVESTIGATIONS

- Urine analysis: for blood, proteins, leucocytes, casts
- Urea, creatinine and electrolytes

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Management of acute kidney condition can be started at hospital level but the patient should be referred at higher level for more appropriate management:
- Treat underlying conditions e.g., dehydration ➔Fluid NS/RL 20ml/kg over 1hours
- Monitor fluid input and output Daily fluid requirements = 10 ml/kg + total of losses through urine, vomitus and diarrhea
- Monitor BP twice daily
- Daily weighing
- Restrict salt intake (<2 g or half teaspoonful daily)
- Restrict potassium intake e.g., oranges, bananas, vegetables, meat, fizzy drinks
- Moderate protein intake
- Ensure adequate calories in diet
- Check urine and electrolytes frequently

Pharmacologic

- Treat any complications (e.g., infections, hypertension, convulsions), adjusting drug dosages according to the clinical response where appropriate

- If oliguria, furosemide IV according to response (high doses may be necessary)
- If no response to above general measures, worsening kidney function or anuria (urine output less than 100 ml/24 hours)
- Refer for specialist management including possible dialysis as soon as possible and before the patient's condition becomes critical

INDICATIONS FOR DIALYSIS

- BUN>150MG/DL I rising
- Referactory edema for medical management
- Severe hyperkalemia refractory to medical treatment

CAUTION

- Do not give any drugs, which may make kidney damage worse e.g. use gentamicin with caution

FURTHER READING

1. Mola K, Shimelis D. Pattern and outcome of renal diseases in hospitalized children in Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia. Ethiopian Medical Journal. 2016 Jun 9;54(3).
2. Gordon DM, Frenning S, Draper HR, Kokeb M. Prevalence and burden of diseases presenting to a general pediatrics ward in Gondar, Ethiopia. Journal of tropical pediatrics. 2013 Oct 1;59(5):350-7.

16.4.3 CHRONIC KIDNEY DISEASE

BRIEF DESCRIPTION

- Chronic impairment of kidney function

CAUSES/RISK FACTORS

- Diabetes mellitus
- Hypertension/cardiovascular disease

- Kidney stones
- Drugs especially pain killers like ibuprofen and other NSAIDs
- Family history of kidney disease HIV/AIDS
- Congenital malformations
- VUR

CLINICAL FEATURES

- Most patients with CKD have no symptoms until the disease is advanced
- May present with features of predisposing risk factor
- Anaemia, lethargy, easy fatigue, appetite loss, nausea, vomiting, skin itching, bone pains
- May have body swelling
- May have loin pain

DIFFERENTIAL DIAGNOSIS

- Other causes of chronic anaemia
- Heart failure
- Protein-energy malnutrition
- Chronic liver disease

INVESTIGATIONS

- Creatinine/Urea/electrolytes
- Urine dip stick for protein and blood
- Kidney ultrasound
- How to screen for CKD in patient at risk
- Urine dipsticks (for protein and blood) and blood pressure measurement at least once a year in high-risk patients
- In diabetics, urine micro albumin where possible or a spot urine for protein:

creatinine ratio at least once a year

- Patients with detected abnormalities should have a serum creatinine test performed and GFR calculated as suggested above
- Refer the following patients for specialist attention:
  - Children
  - Persistent proteinuria or haematuria beyond 3 months
  - GFR <60 ml/min or creatinine >1.9 mg/dl
  - Familial kidney disease, e.g., polycystic kidney disease

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Treatment of end stage renal disease is complex and expensive, and available only at national referral hospital.

Goals

- Establish diagnosis and treat reversible diseases
- Identify co-morbid conditions and manage further complications of CKD
- Slow progression of CKD by optimizing treatment
- Plan renal replacement therapy well before end stage kidney disease is reached

TREATMENT TO PRESERVE KIDNEY FUNCTION IN PATIENTS WITH CKD

- Lifestyle modifications: Weight loss, stop smoking, exercise, healthy balanced diet, lipid control, salt restriction
- Blood pressure control:

  - Target 130/80 mmHg (lower in children).
  - Use ACE inhibitors as first line antihypertensive for diabetics and patients with proteinuria, plus low salt diet
- In diabetics:
  - BP control is paramount:
  - Optimal blood sugar control (HbA1C <7%)
- Proteinuria:
  - Reduce using ACE inhibitors and/or ARBs; target < 1 g/day
- Avoid nephrotoxic medicines, e.g., NSAIDs, celecoxib's, aminoglycosides, contrast agents

PREVENTION OF COMPLICATIONS

- Anemia: due to multiple causes.
  - Consider iron and folic supplements. Target Hb 11-12 gr/dL
- Bone mineral disease:
  - Consider adding calcium lactate or other calcium/vitamin D supplements

TREATMENT OF SYMPTOMS

- If fluid retention/oliguria, furosemide tablet according to response (high doses may be necessary)
- Dialysis for end stage cases

CAUTION

- Start ACE inhibitors at low doses and monitor renal function carefully. DO NOT use in advanced chronic disease

PREVENTION

- Screening of high-risk patients
- Optimal treatment of risk factors

- Treatments to slow progression in initial phases
- Avoidance of nephrotoxic drugs

REFERENCE

1. Harambat J, Van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. Pediatric nephrology. 2012 Mar 1;27(3):363-73.
2. Mola K, Shimelis D. Pattern and outcome of renal diseases in hospitalized children in Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia. Ethiopian Medical Journal. 2016 Jun 9;54(3).

16.5 HEMATOLOGIC DISEASES IN CHILDREN

16.5.1 ANEMIA IN CHILDREN

BRIEF DESCRIPTION

- Anemia is defined as reduction in red blood cell (RBC) mass, which will be measured in the laboratory, by reduction in hemoglobin concentration or hematocrit or RBC count. WHO criteria for anemia.
- For children 6mo-59months <11g/dl, 5yrs-12yrs <11.5g/dl, 12-15yrs <12g/dl, after 15 yrs. adult cut off points are used.
- Anemia is not a single disease entity; it is rather a manifestation of several pathologies.
- The causes of anemia can be divided in to two broad categories
    - Anemia due to increased RBC loss or destruction- Hemorrhage or hemolysis
    - Anemia due to defective or decreased RBC production - Examples – Iron deficiency anemia, B12 or folate deficiency, anemia of chronic disease/chronic renal failure/hypothyroidism, Aplastic anemia, Bone marrow infiltration, Chemotherapy induced anemia.
- Anemia is often a symptom of a disease rather than a disease itself.

CLINICAL FEATURES

- Most symptoms of anemia are a result of the decrease of oxygen in the cells or "hypoxia." Because red blood cells, as hemoglobin, carry oxygen, a decreased production or number of these cells result in "hypoxia." Many of the symptoms will not be present with mild anemia, as the body can often compensate for gradual changes in hemoglobin.
- Common clinical manifestations include easy fatigability, shortness of breath, palpitation, dizziness, vertigo, irritability and loss of appetite. Depending on the underlying cause patients may also have jaundice.
- Physical examination may reveal pallor, tachycardia, atrophy of tongue papillae, swollen edematous togue, systolic ejection murmur, hepatosplenomegaly, bone tenderness and extremity edema.

DIAGNOSIS:

- guided by history, physical examination findings and the likely differential diagnosis considered accordingly
- Complete blood count,
- Reticulocyte count
- Stool examination…. For intestinal parasites, occult blood
- Peripheral morphology
- Additional tests guided by the likely diagnosis

TYPES

- Iron deficiency anemia.
- Megaloblastic (pernicious) anemia.
- Hemolytic anemia.
- Sickle cell anemia.
- Cooley's anemia (thalassemia).
- Aplastic anemia
- Chronic anemia.

TREATMENT

Objectives

- Improve the functional status of anemia
- Prevent development of complications such as Heart failure
- Treatment of the underlying cause

Non-pharmacologic

- Specific treatment for anemia will be determined based on the following:
    - Age, overall health and medical history.
    - The extent of the anemia.
    - Child's tolerance for specific medications, procedures or therapies.
    - Expectations for the course of the anemia.
    - Packed RBC or whole blood transfusion (when there is Heart failure, severe hypoxic symptoms, acute ongoing bleeding)
    - Nutritional support
    - Non pharmacologic treatment pertinent to the underlying cause

PHARMACOLOGIC

- There is no universal pharmacologic treatment for all causes of anemia

COMPLICATIONS

- In general, anemia may cause:
    - Problems with growth and development
    - An enlarged heart, heart failure
    - Megaloblastic anemia can also cause problems with the nervous system.

FURTHER READING

1. Janus J, Moerschel SK. Evaluation of anemia in children. American family physician. 2010 Jun 15;81(12):1462-71.

2. Muchie KF. Determinants of severity levels of anemia among children aged 6–59 months in Ethiopia: further analysis of the 2011 Ethiopian demographic and health survey. BMC Nutrition. 2016 Dec 1;2(1):51.

IRON DEFICIENCY ANEMIA

- Iron deficiency in children is a common problem.
- It can occur at many levels, from a mild deficiency all the way to iron deficiency anemia — a condition in which blood doesn't have enough healthy red blood cells.
- Untreated iron deficiency can affect a child's growth and development.

RISK OF IRON DEFICIENCY

- Perinatal factor: prematurity, low birth weight, fetpmaternal hemorrhage, TTTS
- Dietary factors: low iron bio vailability of iron (cow's milk), poor iron content of diets, diets which decrease bioavailability of iron
- Chronic blood loss:
- Decreased absorption: celiac disease, surgery, CD
- Adolescent girls also are at higher risk of iron deficiency because their bodies lose iron during menstruation.

CLINICAL FEATURE

- Pale skin, fatigue, cold hands and feet, slowed growth and development, poor appetite, abnormally rapid breathing, behavioral problems, frequent infections, unusual cravings for non-nutritive substances, such as ice, dirt, paint or starch

INVESTIGATION

- CBC
- Peripheral blood smear
- Stool examination: stool for occult blood, stool microscopy for hook worm infestation.

- Further investigation will depend on the suspected cause/s of anemia based on the above tests, history and physical examination findings.

PREVENTION

- Delayed cord clamping for 1-3 minutes
- Iron supplementation for pre-terms <35weeks of gestation or birth weight <2000gm starting from 2 weeks of age.
- Limit dietary intake of coms milk in infants to less than 24Oz per day
- Enhancing absorption. Vitamin C helps promote the absorption of dietary iron.

TREATMENT

Objectives

- Improve the functional status of anemia
- Prevent development of complications such as Heart failure
- Treatment of the underlying cause

Non-pharmacologic

- Packed RBC or whole blood transfusion (when there is Heart failure, severe hypoxic symptoms, acute ongoing bleeding)
- Nutritional support
- Non pharmacologic treatment pertinent to the underlying cause

PHARMACOLOGIC

- **Oral iron replacement**

First line

- **Ferrous sulphate,** elemental iron 3-6mg/kg/day, treatment has to be continued for 2-3months after Hemoglobin has normalized

N.B. The cause of the iron deficiency state should be identified and treated

FURTHER READING

1. Desalegn A, Mossie A, Gedefaw L. Nutritional iron deficiency anemia: magnitude and its predictors among school age children, southwest Ethiopia: a community based cross-sectional study. PloS one. 2014 Dec 1;9(12):e114059
2. Woldie H, Kebede Y, Tariku A. Factors associated with anemia among children aged 6–23 months attending growth monitoring at Tsitsika Health Center, Wag-Himra Zone, Northeast Ethiopia. Journal of nutrition and metabolism. 2015 May 27;2015.

MEGALOBLASTIC ANEMIA

- In megaloblastic anemia, the bone marrow, where the cells are formed, makes fewer cells. And the cells that are formed don't live as long as normal. The red blood cells are:
    - Macrocytosis,
    - Ovalocytotis,
    - neutrophil hypersegmentation

CAUSE

- There are many causes of megaloblastic anemia. The most common cause in children is lack of folic acid or vitamin B-12. Other causes include:
    - **Digestive diseases:** Malabsorption syndromes, infectious enteritis, pernicious anemia, surgery
    - **Inherited congenital folate malabsorption:** A genetic problem in which infants can't absorb folic acid.
    - **Medicines.** Phenytoin, metformin, ARV drugs
    - **Diet:** Vegetarian diet, goat milk ingestion

CLINICAL FEATURES

- The symptoms of megaloblastic anemia may look like other conditions or medical problems.
- These are some of the symptoms of megaloblastic anemia:

- Pale or yellow skin, Fast heart beat
- Shortness of breath
- Lack of energy, feeling tired, decreased appetite
- Irritability or fussiness, hair color changes
- Stomach upsets, nausea, diarrhea, gas, constipation
- Trouble walking, Numbness or tingling in hands and feet, muscles weakness
- Smooth and sore tongue glossitis

DIAGNOSIS

- The healthcare provider will ask about your child's symptoms and health history. He or she will give your child a physical exam. Your child may also have tests, such as:
  - Hemoglobin and hematocrit.
  - Complete blood count, or CBC.
  - Peripheral smear. Check to see ovalocytosis, hypersegemented neutrophils
  - **Other test:** S/E, a bone marrow aspiration, biopsy, or both may be done. Barium study

TREATMENT

Objectives

- Improve the functional status of anemia
- Prevent development of complications such as Heart failure
- Treatment of the underlying cause

Non-pharmacologic

- Most children with megaloblastic anemia are given B-12 or folic acid supplements.

- Foods that have natural folate include: Oranges, Dark green and leafy vegetables, Liver, Barley, Beans, peas, lentils, Peanuts, Cereals, breads, pastas, and rice are fortified with man-made folic acid. Meat and dairy products have the most vitamin B-12.

PHARMACOLOGIC

- **Pharmacologic treatment of megaloblastic anemia – Cyanocobalamin (Vitamin B12),** 1000 micrograms (1mg), IM, every day for one week, every week for four weeks and then, **if the underlying disorder persists**, 1 mg every month for the remainder of the patient's life**.**

- **Pharmacologic treatment of megaloblastic anemia- Folate deficiency Folic acid**, 1 to 5 mg p.o. daily for 1- 4 months, or until complete hematologic recovery occurs.

FURTHER READING

1. Bhatia P, Kulkarni JD, Pai SA. Vitamin B12 deficiency in India: Mean corpuscular volume is an unreliable screening parameter. The National medical journal of India. 2012 Jan 1;25(6):336-8.

2. Chandra J. Megaloblastic anemia: back in focus. The Indian Journal of Pediatrics. 2010 Jul 1;77(7):795-9.

16.5.2 THROMBOCYTOPENIA

- Defined as a platelet count of less than 150,000/microL.

- Many things can cause thrombocytopenia in children, most commonly infections (especially viral infections) and destruction of platelets by the immune system (called immune thrombocytopenia or ITP).

IMMUNE THROMBOCYTOPENIA

- Immune thrombocytopenic purpura (ITP) or idiopathic thrombocytopenic purpura is a common acquired bleeding disorder.

- It is characterized by isolated thrombocytopenia while the rest of the complete blood count is entirely normal, unless other coincidental abnormalities are present, such as iron deficiency.

- Clinically apparent associated conditions (e.g., systemic lupus erythematosus) should be excluded to make the diagnosis of ITP. Patients with these associated conditions are described as having secondary immune thrombocytopenia.
- The incidence of ITP is higher in children than adults. Preceding viral infections are common precipitants.

CLINICAL FEATURES

- Petechiae, purpura, and easy bruising.
- Epistaxis, gingival bleeding, and menorrhagia.
- Gastrointestinal bleeding and gross hematuria
- Intracranial hemorrhage.
- The bleeding of thrombocytopenia is mucocutaneous, as opposed to the delayed, deep seated hematomas characteristic of coagulation disorders such as hemophilia
- The clinical manifestations of thrombocytopenia vary with age. Older patients may have more severe bleeding manifestations, such as gastrointestinal bleeding and possibly intracranial hemorrhage because of comorbidities such as hypertension.

INVESTIGATIONS

- CBC
- Peripheral blood smear (to exclude other causes of thrombocytopenia)
- Serology for HIV, HCV (hepatitis C Virus).

Treatment – refer to specialist

FURTHER READING

1. Melboucy-Belkhir S, Khellaf M, Augier A, Boubaya M, Levy V, Le Guenno G, Terriou L, Lioger B, Ebbo M, Morin AS, Chauveheid MP. Risk factors associated with intracranial hemorrhage in adults with immune

thrombocytopenia: a study of 27 cases. American Journal of Hematology. 2016 Dec;91(12):E499-501.

2. D'Orazio JA, Neely J, Farhoudi N. ITP in children: pathophysiology and current treatment approaches. Journal of pediatric hematology/oncology. 2013 Jan 1;35(1):1-3.

THROMBOTIC THROMBOCYTOPENIC PURPURA AND HEMOLYTIC UREMIC SYNDROME (TTP/HUS)

- Hemolytic-uremic syndrome consists of the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure.
- Hemolytic-uremic syndrome shares many features with thrombotic thrombocytopenic purpura (TTP).
- Both diseases include multiorgan dysfunction due to thrombotic microangiopathy, with active hemolysis and thrombocytopenia.

CAUSES

STEC-HUS

- GI tract infection with Stx–producing E coli (STEC) precedes most cases of STEC-HUS. Stx1 is identical to the Stx produced by Shigella dysenteriae.
- Other causes of hemolytic-uremic syndrome include infection by the following:
    - o *S.dysenteriae* (established as an etiologic agent)
    - o *Salmonella typhi* (established as an etiologic agent)
    - o *Bacteroides* species
    - o *Entamoeba histolytica*
    - o *Aeromonas hydrophilia*
- Causes of a HUS include the following:
    - o Inherited (e.g., mutations in the gene for factor H, a complement regulatory protein)

  - *S. pneumoniae* (neuraminidase-associated)
  - Portillo virus
  - Coxsackie virus
  - Influenza virus
  - Epstein-Barr virus

Laboratory studies

- Complete blood count
- Peripheral morphology
- Serum chemistry: Renal function test, serum electrolyte
- Fibrin degradation products (if available)
- Classic findings in hemolytic-uremic syndrome (HUS) include anemia and thrombocytopenia, with fragmented RBCs

Diagnosis

- Clinical one and is not excluded by a negative stool culture.

TREATMENT

Objectives

- Early recognition of cases and planning appropriate management
- Prevent development of life-threatening complications
- Treatment of the underlying cause

Non-pharmacologic

- Successful management of hemolytic-uremic syndrome (HUS) begins with early recognition of the disease and supportive care.
- Good control of volume status, electrolyte abnormalities, hypertension, and anemia.
- Possible referral of cases with altered mentation and renal insufficiency.

PHARMACOLOGIC

- Early and ample hydration with intravenous isotonic saline is associated with a lower risk of progression to oligoanuric hemolytic-uremic syndrome in patients with diarrhea

FURTHER READING

1. Kiss JE. Thrombotic thrombocytopenic purpura: recognition and management. International journal of hematology. 2010 Jan 1;91(1):36-45.
2. Scully MA. The pathogenesis of thrombotic thrombocytopenic purpura. University of London, University College London (United Kingdom); 2008.

16.5.3 HEMOPHILIA

- Hemophilia is an X linked inherited bleeding disorder related to clotting factor deficiency.

TYPES

- The 3 main forms of hemophilia include:
  - **Hemophilia A.** This is caused by a lack of the blood clotting factor VIII. About 9 out of 10 people with hemophilia have type A disease. This is also referred to as classic hemophilia.
  - **Hemophilia B.** This is caused by a deficiency of factor IX. This is also called Christmas disease or factor IX deficiency.
  - **Hemophilia C.** Some doctors use this term to refer to a lack of clotting factor XI.

CAUSE

- Hemophilia types A and B are inherited diseases. They are passed on from parents to children through a gene on the X chromosome. Females have 2 X chromosomes, while males have 1 X and 1 Y chromosome.
- A female carrier has the hemophilia gene on 1 of her X chromosomes. When a hemophilia carrier female is pregnant, there is a 50/50 chance that the hemophilia gene will be passed on to the baby.

  - If the gene is passed on to a son, he will have the disease.
  - If the gene is passed on to a daughter, she will be a carrier.
- If the father has hemophilia but the mother does not carry the hemophilia gene, then none of the sons will have hemophilia disease, but all of the daughters will be carriers.
- In about 1/3 of the children with hemophilia, there is no family history of the disorder. In these cases, it's believed that the disorder could be related to a new gene flaw.
- Carriers of the hemophilia gene often have normal levels of clotting factors but may:
  - Bruise easily
  - Bleed more with surgeries and dental work
  - Have frequent nosebleeds
  - Have heavy menstrual bleeding
- Hemophilia C usually doesn't cause problems, but people may have increased bleeding after surgery.

CLINICAL FEATURES

- The most common symptom of this disorder is heavy, uncontrollable bleeding. Patients may bruising, bleeding following even trivial trauma, bleeding in joint (hemarthrosis) and muscles or intracranial hemorrhage.
- The severity of hemophilia depends on the amount of clotting factors in the blood. Those affected with hemophilia that have levels greater than 5% (100% being average for unaffected children) most often have bleeding only with major surgeries or tooth extractions.
- Severe hemophilia is when the factor VIII or IX is less than 1%.
- In any active toddler any hot tender joint should be investigated for hemophilia
- Bleeding can occur in these children, even with the minimal activities of

daily life. Bleeding may also occur from no known injury. Bleeding most often occurs in the joints and in the head.

- **Other bleeding.** Blood found in the urine or stool may also signal hemophilia.
- The symptoms of hemophilia may look like other problems.

DIAGNOSIS

- The diagnosis of hemophilia is based on family history of bleeding disorder, child's medical history, and a physical exam.
- Blood tests include:
  - Complete blood count (CBC), coagulation profile
  - Clotting factors. bleeding times.
  - Genetic or DNA testing.

TREATMENT

Objectives

- Early recognition and referral for specialist evaluation.
- Prevent development of life-threatening complications
- Promote growth of the child

Non-pharmacologic

- Treatment will depend on the child's symptoms, severity of symptom, age, and general health.
- Bleeding in the joint may need surgery or immobilization.
- Physical therapy and exercise to strengthen the muscles around the area.
- Blood transfusions may be needed if major blood loss has occurred.

Pharmacologic

- Factor VIII or IX can allow a child with hemophilia to lead a near normal lifestyle.

COMPLICATIONS

- Long-term joint problems
- Very serious tumor-like enlargements, of the muscle and bone
- Development of antibodies against clotting factors.
- Infections from transfusions (HIV and hepatitis B and C are no longer spread through donated blood)

FURTHER READING

1. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, Ludlam CA, Mahlangu JN, Mulder K, Poon MC, Street A. Guidelines for the management of hemophilia. Haemophilia. 2013 Jan;19(1):e1-47.

16.5.4 TRANSFUSION IN CHILDREN

- A blood transfusion is when blood is put into the body through this IV line.

TYPES OF BLOOD

- People with O− blood do not have A, B, or Rh molecules on their blood cells. These people can donate blood to anyone, and are known as universal donors.
- People who are AB+ have all 3 molecules (A, B, and Rh) on their blood cells and can safely receive blood from anyone.
- Other blood types can donate and give to only their matching blood types.

INDICATION OF BLOOD TRANSFUSION

- A serious injury that's caused major blood loss
- Surgery that's caused a lot of blood loss
- A liver problem that makes the body unable to create certain blood parts
- A bleeding disorder such as hemophilia
- An illness that causes reduced or poor-quality RBCs (anemia)

- Kidney failure, which causes problems with blood cell production
- Treatment for cancer (chemotherapy) that slows down the body's production of blood cells

PREPARATION FOR TRANSFUSION

- Child's blood may be tested before the blood transfusion to find out what type it is. This is to make sure that your child gets the right kind of donor blood.
- Cross match

PROCEDURE

A. Volume of blood to transfused: 20ml/kg over 2-4hours

B. If patients has Heart failure 10ml/kg over 2-4 hours

C. No need to ward.

D. No need to give diuretics if transfusion is being given for volume expansion.

E. Do not administer medication in the same line blood is being given.

F. Patient should be kept NPO during transfusion and for at least for 3hours.

COMPLICATIONS OF TRANSFUSION

- All procedures have some risks.
- The risks of blood transfusions include:
    - An allergic reaction. These symptoms may start soon after a blood transfusion or within the next 24 hours.
    - Fever. This can happen within a day of the blood transfusion. It's usually temporary.
    - Destruction of red blood cells by the body (hemolytic reaction).
    - Volume overload.

  - Too much iron in the body (iron overload).
  - Infection associated with transfusion Viruses being transmitted.
  - Graft versus host disease.
  - Transfusion associated lung injury (TRALI)

REFERENCE

- Stainsby D, Jones H, Wells AW, Gibson B, Cohen H, SHOT Steering Group. Adverse outcomes of blood transfusion in children: analysis of UK reports to the serious hazards of transfusion scheme 1996–2005. British journal of hematology. 2008 Apr;141(1):73-9.

16.6 RHEUMATOLOGIC DISEASES IN CHILDREN

16.6.1 JUVENILE RHEUMATOID ARTHRITIS

BRIEF DESCRIPTION

- Juvenile rheumatoid arthritis (JRA) is the most common chronic rheumatologic disease in children and is one of the most common chronic diseases of childhood.
- The etiology is unknown, and the genetic component is complex, making clear distinctions between the various subtypes difficult.
- A new nomenclature, juvenile idiopathic arthritis (JIA), is being increasingly used to provide better definition of subgroups.

CLINICAL FEATURES

- History findings in children with JIA may include the following:
  - Arthritis present for at least 6 weeks before diagnosis (mandatory for diagnosis of JIA)
  - Either insidious or abrupt disease onset, often with morning stiffness or gelling phenomenon and arthralgia during the day

  - Complaints of joint pain or abnormal joint use
  - History of school absences or limited ability to participate in physical education classes
  - Spiking fevers occurring once or twice each day at about the same time of day
  - Evanescent rash on the trunk and extremities
  - Psoriasis or more subtle dermatologic manifestations
- Physical findings are important to provide criteria for diagnosis and to detect abnormalities suggestive of alternative etiologies, as well as to indicate disease subtypes.
- Such findings include the following:
  - Arthritis: Defined either as intra-articular swelling on examination or as limitation of joint motion in association with pain, warmth, or erythema of the joint; physical findings in JIA reflect the extent of joint involvement
  - Synovitis: Characterized by synovial proliferation and increased joint volume; the joint is held in a position of maximum comfort, and range of motion often is limited only at the extremes

TYPES OF JIA INCLUDE THE FOLLOWING:

- Systemic-onset juvenile idiopathic arthritis
- Oligoarticular juvenile idiopathic arthritis
- Polyarticular juvenile idiopathic arthritis
- Psoriatic arthritis
- Enthesitis-related arthritis
- Undifferentiated arthritis

DIAGNOSIS

- Diagnosis of JIA is based on the history and physical examination findings.

- When physical findings do not document definite arthritis, further evaluation is warranted.
  - CBC, Acute phase reactant. ESR
  - Rheumatoid factor, ASO TITER, LFT, RFT, ANA titer
  - X- ray, Joint Ultrasound

TREATMENT

Objectives

- Achieve disease remission
- Prevent development of chronic complications
- Promote growth of the child

Non-pharmacologic

- A team-based approach to the treatment of JIA can be helpful.
- Psychosocial interventions
- Measures to enhance school performance (eg, academic counseling)
- Dietary evaluation and counseling to ensure adequate intake of calcium, vitamin D, protein and calori.
- Physical therapy
- Additional measures:
  - Periodic slit-lamp examination…referral for ophthalmologic evaluation if not available.
  - Orthopedic consultation for patients with leg-length discrepancy, FFD of joints, scoliosis.

Pharmacologic

- When to use these agents have to be specified:
  - **NSAIDs:** as initial therapy for patients with JIA excepts those patients who have severe disease and functional limitation at presentation

    - Continue for 4-6 weeks before adding another agent
- ○ **Intraarticular steroids**: for patients
    - Who show no response after 4-6 weeks of NSAID treatment
    - Functional limitation like JC or LLD at presentation
- ○ **DMARDs:**
    - For patient who show no response to NSAID + intraarticular steroid treatment
    - Methotrexate 0.5-1mg/kg po/sc weekly
- ○ **Systemic steroids:** indications
    - Severe JIA
    - Bridge therapy; the wait for therapy with DMARDs
    - Control of uveitis
- ○ **Biologic agents:**
    - For patients who have no response to DAMRDS (which may take 6-12 weeks)
    - **Indication for treatment**
        - ✓ A history of arthritis in 4 or fewer joints
        - ✓ A history of arthritis in 5 or more joints
        - ✓ Active sacroiliac arthritis
        - ✓ Systemic arthritis without active arthritis
    - Systemic arthritis with active arthritis

FURTHER READING

1. April KT, Feldman DE, Platt RW, Duffy CM. Comparison between children with juvenile idiopathic arthritis (JIA) and their parents concerning perceived quality of life. Quality of Life Research. 2006 May 1;15(4):655-61.

2. April KT, Feldman DE, Platt RW, Duffy CM. Comparison between children with juvenile idiopathic arthritis (JIA) and their parents concerning perceived quality of life. Quality of Life Research. 2006 May 1;15(4):655-61.

16.6.2 HENOCH-SCHÖNLEIN PURPURA (HSP)

BRIEF DESCRIPTION

- Henoch-Schonlein purpura (also known as IgA vasculitis) is a disorder that causes small blood vessels in your skin, joints, intestines, and kidneys to become inflamed and bleed.
- The most striking feature of this form of vasculitis is a purplish rash, typically on lower legs and buttocks.
- Henoch-Schonlein purpura can also cause abdominal pain and aching joints.
- Rarely, serious kidney damage can occur.
- Henoch-Schonlein purpura can affect anyone, but it's most common in children between the ages of 2 and 6.
- The condition usually improves on its own.
- Medical care is generally needed if the disorder affects the kidneys.

CLINICAL FEATURES

- The four main characteristics of Henoch-Schonlein purpura include:
    - **Palpable Rash (purpura).** Reddish-purple spots that look like bruises develop on the buttocks, legs and feet. The rash can also appear on the arms, face and trunk and may be worse in areas of pressure, such as the sock line and waistline.
    - **Swollen, sore joints (arthritis).**
    - **Digestive tract symptoms.**
    - **Kidney involvement.**

CAUSES

- In Henoch-Schonlein purpura, some of the body's small blood vessels become inflamed, which can cause bleeding in the skin, abdomen and kidneys.
    - It's not clear why this initial inflammation develops.
    - It may be the result of the immune system responding inappropriately to certain triggers.
- Nearly half the people who have Henoch-Schonlein purpura developed it after an upper respiratory infection, such as a cold.
- Other triggers include chickenpox, strep throat, measles, hepatitis, certain medications, food, insect bites and exposure to cold weather.

Risk factors

- Factors that increase the risk of developing Henoch-Schonlein purpura include:
    - **Age.** The disease affects primarily children and young adults, with the majority of cases occurring in children between the ages of 2 and 6.
    - **Sex.** Henoch-Schonlein purpura is slightly more common in males than in females.
    - **Race.** White and Asian children are more likely to develop Henoch-Schonlein purpura than are black children.

COMPLICATIONS

- For most people, symptoms improve within a month, leaving no lasting problems. But recurrences are fairly common.
- Complications associated with Henoch-Schonlein purpura include:
    - **Kidney damage.** The most serious complication of Henoch-Schonlein purpura is kidney damage. This risk is greater in adults than in children. Occasionally the damage is severe enough that dialysis or a kidney transplant is needed.

- **Bowel obstruction.** In rare cases, Henoch-Schonlein purpura can cause intussusception — a condition in which a section of the bowel folds into itself like a telescope, which prevents matter from moving through the bowel.

DIAGNOSIS

- Clinical: classic rash, joint pain and digestive tract symptoms are present.

LABORATORY TESTS

- No single laboratory test can confirm Henoch-Schonlein purpura, but certain tests can help rule out other diseases and make a diagnosis of Henoch-Schonlein seem likely.
- They may include:
    - **Blood tests.**
    - **Urine tests.** for evidence of blood, protein or other abnormalities.
    - **Biopsies:** People who have Henoch-Schonlein purpura often have deposits of a certain protein, IgA (immunoglobulin A), on the affected organ.
    - **Imaging tests:** rule out other causes of abdominal pain and to check for possible complications, such as a bowel obstruction.

TREATMENT

Objectives

- To shorten the duration of symptom

Non-pharmacologic

- Henoch-Schonlein purpura usually goes away on its own within a month with no lasting ill effects. Rest, plenty of fluids and over-the-counter pain relievers may help with symptoms.
- Surgery
- If a section of the bowel has folded in on itself or ruptured, surgery may be needed.

Pharmacologic

- Corticosteroids, such as prednisone, may help shorten the time and intensity of joint and abdominal pain.
- Because drugs can have serious side effects, outweigh the risks and benefits of using this drug.

FURTHER READING

1. Chen P, Zhu XB, Ren P, Wang YB, Sun RP, Wei DE. Henoch Schonlein Purpura in children: clinical analysis of 120 cases. African health sciences. 2013 Apr 12;13(1):94-9.
2. Bluman J, Goldman RD. Henoch-Schönlein purpura in children: limited benefit of corticosteroids. Canadian Family Physician. 2014 Nov 1;60(11):1007-10.

16.7 CARDIOVASCULAR DISEASES IN CHILDREN

16.7.1 CONGENITAL HEART DISEASE (CHD)

BRIEF DESCRIPTION

- In children, cardiac failure is most often caused by congenital heart disease and cardiomyopathy.
- These causes are significantly different from those usually responsible for the condition in adults, which include coronary artery disease and hypertension.

RISK FACTORS FOR CONGENITAL HEART DISEASE

- Maternal conditions:
    - Infection during pregnancy: rubella, CMV, herpes viruses, HIV maternal
    - Drug use: phenytoin, valproate, estrogen, progesterone, trimethadione,

lithium, ACE inhibitors

  - Alcohol consumption and smoking of cigarettes during pregnancy
  - Medical illness: maternal diabetes mellitus
- Neonatal condition: prematurity and low birth weight, large for gestational age babies, chromosomal aberrations,

EVALUATION AND SCREENING OF INFANTS AND CHILDREN FOR CONGENITAL HEART DISEASE

- The initial evaluation of suspected congenital heart disease involves a systemic approach with **three** major components.
- Classify congenital heart diseases as **Cyanotic or Acyanotic:** based on the finding on physical examination aided by pulse oximetry.
- Determine whether the pulmonary blood flow is increased, normal or decrease on chest X-ray: help to narrow the differential diagnosis.
- Determine the physiologic load of the defect on the cardiac chambers by using ECG: shows presence or absence of chamber enlargement and hyperthrophies.

CLINICAL FEATURES

- Some have no symptoms
- The symptoms of congenital heart disease in infants and children may include:
  - Cyanosis, fast breathing and poor feeding, poor weight gain
  - Lung infections, in inability to exercise
  - Unusual sound or heart murmur

DIAGNOSIS

- The final diagnosis can be established by echocardiography.
- Cardiac catheterization, cardiac MRI and CT scan also be used when available.

- Chest X-ray: These can reveal signs of heart failure
- Electrocardiogram ECG or EKG: This measures the heart's electrical activity.

TREATMENT

Objectives

- Prevent development of complications such as Heart failure
- Treatment of the underlying cause

Non-pharmacologic

- Good dental hygiene Take good care of teeth and gums to prevent infections.
- Antibiotics before you have any medical work that may cause bleeding, like dental work and most surgeries.
- Regular cardiac follow-up
- Refer for specialist evaluation➔Patient may need medications, surgery, or other procedures

FURTHER READING

1. Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality resulting from congenital heart disease among children and adults in the United States, 1999 to 2006. Circulation. 2010 Nov 30;122(22):2254-63.
2. Nigussie B, Tadele H. Heart failure in Ethiopian children: Mirroring the unmet cardiac services. Ethiopian Journal of Health Sciences. 2019;29(1).

CYANOTIC CONGENITAL HEART DISEASE WITH HYPOXEMIC ATTACKS/SPELLS

- Sudden severe episodes of intense cyanosis caused by reduction of pulmonary flow in patients with underlying Tetralogy of Fallot or other cyanotic heart lesions.

- **Common cardiac lesions associated with Hyper cyanotic spell are:**
    - Tetralogy of Fallot
    - Pulmonary atresia
    - Tricuspid atresia with pulmonary stenosis.
    - Transposition of Great arteries with pulmonary stenosis
    - Single ventricle physiology with PS or pulmonary atresia

CLINICAL FEATURES

- Peak incidence age: 3 to 6 months.
- Often in the morning.
- Severe cyanosis, hyperpnoea, metabolic acidosis.
- In severe cases, may lead to syncope, seizure, stroke or death.
- There is a reduced intensity of systolic murmur during spell due to reduce pulmonary blood flow
- Irritability due to acute cerebral hypoxia
- CXR usually shows oligaemic lungs

TREATMENT

Objectives

- Improve the functional status of anemia
- Prevent development of complications such as heart failure, hypoxic ischemic injury
- Treatment of the underlying cause

Non-pharmacologic

- Keep the child calm, Place the baby on the mother’s shoulder with the knees tucked up underneath.

- This provides, reduces systemic venous return and increases systemic vascular resistance.
- Posture: knee-chest position
- Avoid painful procedures before sedating the patient

Pharmacologic

- Facemask oxygen (make sure the patient is not agitated more due to the face mask)
- Sedation: morphine 0.1 - 0.2 mg/kg IM/IV/SC or ketamine (2 - 4 mg/kg IM or 1 - 2 mg/kg IV) – repeat as necessary
- Blood volume expansion: 10 ml/kg 0.9% saline IV bolus and repeat as necessary to increase preload.
- Beta-blocker: propranolol 0.05 –0.1 mg/kg IV slow bolus over 10 min
- Sodium bicarbonate 1 - 2 mmol/kg IV
- If there is infection: treat accordingly
- If no response refers to specialist

FOLLOW UP:

- continuous monitoring of vital signs, oxygen saturation and level of consciousness,
- check for murmur,
- Acid base gas analysis (if available)

DISCHARGE PLAN:

- Oral propranolol 0.2 – 1 mg/kg/dose 8 to 12 hourly
- Iron supplementation dose depends on the degree of anemia
- Appointment to cardiac follow up clinic

16.7.2 ENDOCARDITIS, INFECTIVE

Brief description

- An infection of the endocardium by microorganisms, usually bacterial, rarely fungal.
- Common etiologic agents include staphylococcus aureaus, viridians streptococci and enterococci spp.
- Other causes include HACEK group, Hemophilus influenzae, streptococcus pneumoniae, CONS
- It is classified into 3 types:
    - Sub-acute endocarditis: caused by low virulence organisms such as Streptococcus viridans
    - Acute endocarditis: caused by common pyogenic organisms such as Staphylococcus aureus
    - Post-operative endocarditis: following cardiac surgery and prosthetic heart valve placement. The most common organism involved is Staphylococcus aureus.

RISK FACTORS

- Rheumatic heart disease, congenital heart disease
- Prosthetic valve
- Invasive dental/diagnostic/surgical procedures (including cardiac catheterization)
- Immunosuppression
- IV drug use/abuse

Note: Any unexplained fever in a patient with a heart valve problem should be regarded as endocarditis

CLINICAL FEATURES

- Disease may present as acute or chronic depending on the microorganism involved and patient’s condition

- Fatigue, weight loss
- Low grade fever and chills or acute severe septicemia
- Embolic phenomena affecting various body organs (e.g., brain)
- Heart failure, prominent and changing heart murmurs
- Splenomegaly, hepatomegaly
- Anemia
- Splinter hemorrhages (nail bed and retina)
- Finger clubbing
- Diagnostic triad: persistent fever, emboli, changing murmur

DIFFERENTIAL DIAGNOSIS

- Cardiac failure with heart murmurs
- Febrile conditions associated with anemia

INVESTIGATIONS

- Blood cultures: These are usually positive and all efforts should be made to identify the responsible pathogen and obtain sensitivity data
- At least 3 sets of blood cultures (2-8 ml) each should be obtained (each from a separate venipuncture) at least one hour apart
- Blood: Complete blood count, ESR
- Urinalysis for microscopic hematuria, proteinuria
- Echocardiography
- ECG

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Bed rest
- Treat complications e.g., heart failure
- Follow up with SBE follow up chart

Pharmacologic

- Initial empirical antibiotic therapy
- Ampicillin 100mg/kg/dose IV QID for 4 weeks
- Plus, gentamicin 1 mg/kg IV every 8 hours for 2 weeks

Alternative:

- Ceftriaxone 100mg/kg/ day (maximum 2gm) as in 2 divided doses IV PLUS
- Gentamycin 3mg/kg/day IV
- If staphylococcus suspected, (acute onset) add: Cloxacillin 50 mg/kg IV every 6 hours for 4 weeks
- If the patient didn't respond for the above regimen consider coverage or for children who have prosthetic valve coverage for MRSA (Multi-Resistant Staphylococcus aureus)
- Vancomycin 10 mg/kg (infused over 1 hour) 6 hourly for 6 weeks history of IV antibiotic use within previous 3 months, structural lung damage (Bronchiectasis, COPD, lung fibrosis), prior co-morbidities (cancer, advanced liver or renal disease, immunocompromised), known MRSA carrier
- Once a pathogen has been identified: Amend treatment to correspond with the sensitivity results.
- Patients who show a poor response option of referral for a possible specialist evaluation should be considered

PREVENTION:

- Antibiotic prophylaxis should be considered for patients at highest risk for IE:

- Patients with any prosthetic valve, including atranscatheter valve, or those in whom any prosthetic material was used for cardiac valve repair.
- Patients with a previous episode of IE.
- Patients with CHD:
    - Any type of cyanotic CHD.
    - Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains

- Antibiotic prophylaxis is not recommended in other forms of valvular or CHD

PROCEDURE REQUIRE PROPHYLAXIS

- Dental procedures:
    - Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa.
    - Non- dental procedures:
    - Systematic antibiotic prophylaxis is not recommended for non-dental procedures.
        - Antibiotic therapy is only needed when invasive procedures are performed in the context of infection
        - Amoxicillin 50 mg/kg for children as a single dose, 1 hour before the procedure.

FURTHER READING

1. Moges T, Gedlu E, Isaakidis P, Kumar A, Van Den Berge R, Khogali M, Mekasha A, Hinderaker SG. Infective endocarditis in Ethiopian children: a hospital based review of cases in Addis Ababa. The Pan African Medical Journal. 2015

2. Nigussie B, Tadele H. Heart failure in Ethiopian children: Mirroring the unmet cardiac services. Ethiopian Journal of Health Sciences. 2019;29(1).

16.7.3 RHEUMATIC FEVER, ACUTE

BRIEF DESCRIPTION

- Acute rheumatic fever is a condition, generally classified as connective tissue disease or collagen vascular disease.
- It follows group A beta-hemolytic streptococcal throat infection by a latency period of about 3 weeks.
- It is the most common cause of acquired heart disease in children in developing countries.

DIAGNOSTIC CRITERIA (REVISED JONES CRITERIA)

- Evidence of recent streptococcal infection - Elevated ASO-titer or other streptococcal Ab titres or positive throat swab for group A beta-hemolyticus streptococcus PLUS
- Two major manifestations or one major and two minor manifestations

MAJOR MANIFESTATIONS

- Carditis (occurs in about 50-60% of patients. It affects all the layers of the heart (endocardium, myocardium and pericardium).
- Migratory Polyarthritis
- Erythema marginatum
- Subcutaneous nodules
- Sydehnam's chorea

MINOR MANIFESTATIONS

- Arthralgia
- Fever >380C

- Acute phase reactants (increased ESR/CRP)
- ECG: prolonged PR interval

Note:

- Diagnosis of acute rheumatic fever is established with: 2 major criteria or 1 major and 2 minor criteria and supporting evidence for antecedent streptococcal pharyngitis (mandatory).
- Strict adherence to Jones criteria is not needed under the following situations:
    - Sydenham's chorea
    - Indolent carditis
    - Rheumatic fever recurrence
- Polyarthralgia or monoarthritis can be taken as major criteria in moderate-high risk population (population stratum is based on incidence of RF in school age children or prevalence of RHD in all ages
- Diagnosis of recurrence: 2 major, or 1 major+ 2 minor, or 3 minors (in moderate-high risk population) plus evidence of preceding GAS infection

Investigations

- Blood: Haemogram (raised ESR) or C-reactive protein (CRP)
- Chest X-ray, ECG, Echocardiography
- If it is available, Antistreptolysin O(ASO) titer, Culture from throat swab

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complication

Non-pharmacologic

- Place on bed rest and monitor for evidence of carditis

- Withhold anti-inflammatory treatment till full clinical pictures appear
- Emotional support, especially crucial when Sydenham's chorea is present
- Counseling of the child and family on the nature of the disease, long-term management, prognosis and prevention of recurrence

Pharmacologic

- To eradicate any streptococci:
  - Benzathine benzylpenicillin dose Child < 30 kg: 0.6 MU IM stat, Child > 30 kg: 1.2 MU IM stat
  - **Alternative** (considered when patient is hypersensitive to penicillin)
    - **Erythromycin** 40mg/kg/24 orally divided into 2-4 doses for 4 days *OR*
    - **Azithromycin** 500mg orally on the first day, then 250mg daily for 4 days.

To treat the inflammation

Anti-rheumatic treatment

- Migratory polyarthritis and carditis without cardiomegaly: Aspirin 100mg/kg/24 hours divided into 4 doses, orally for 3-5 days, then 75mg/kg/24hours for 4 weeks.
- Carditis with cardiomegaly or congestive Heart Failure: prednisolone 2mg/kg/24hours divided into 4 doses orally for 2-3 weeks, and while tapering prednisolone, start Aspirin 75mg/kg/24 hours in 4 divided doses for 6 weeks.
- If chorea: Valproate 10-20 mg/kg/day
- Secondary prophylaxis for RF has to be started for all patients with Sydenham's chorea
- Phenobarbital 15-30mg po Q6-8 hrs
- Other alternatives: valproate, haloperidol, chlorpromazine, steroids

PROPHYLAXIS

- To prevent further Benzathine benzylpenicillin 1.2 MU IM every 4 weeks, Child <30 kg: 0.6 MU
- If allergic to penicillin: Erythromycin 10 mg/kg twice a day
- Duration of prophylaxis depends on severity of disease: Rheumatic fever without carditis: for 5 years or until age 18 or 21 years old. Carditis but no residual heart disease: for 10 years or until age 25 years old. Carditis with residual heart disease: untill age 40- 45 years or for life.

PREVENTION

- Early diagnosis and treatment of group A Streptococcus throat infection
- Avoid overcrowding, good housing
- Good nutrition

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16.7.4 HEART FAILURE

ACUTE HEART FAILURE, WITH PULMONARY EDEMA

- Heart failure is a clinical syndrome resulting from the inability of the heart to meet the metabolic and circulatory demands of the body.

COMMON CAUSES HEART FAILURE IN CHILDREN

- Left to right shunt and regurgitant lesions
- Primary myocardial dysfunction such as myocarditis, cardiomyopathy
- Ductal dependent lesions such as Hypo plastic left heart syndrome, severe coarctation of the aorta or interruption of the aortic arch.
- Single ventricle with no stenosis

CLINICAL FEATURES

- The most common signs of Heart Failure, on examination, are:
    - Irritability (baby become calmer as held against the shoulder of the mother), diaphoresis, poor feeding, failure to thrive.
    - In older children
        - Fatigue, exercise intolerance dyspnea, chest pain, syncope

Physical examination

- Tachycardia, cardiomegaly, hepatomegaly
- Poor perfusion cool extremities, delayed distal capillary refill.
- Murmur depends on the cause of underlying cardiac lesion.
- Hyperactive precordium, precordial bulge.
- Hepatomegaly, Wheezing, ± Cyanosis

Investigations

- Confirmation of diagnosis of heart failure and identification of the etiology:
    - Chest x-ray: May show cardiomegaly, pulmonary congestion or frank pulmonary edema.
    - ECG may suggest arrhythmias or structural heart diseases as a cause of Heart Failure.
    - Echocardiography will establish the cause of Heart Failure and gives

structural as well as functional details of the heart

- Assessment of co-morbidities and or precipitating factors CBC, blood culture, electrolyte, and renal function test.

TREATMENT

Objectives

- Relieve congestion by removing excess retained fluid
- Augment contractility
- Reduce after load
- Improve tissue perfusion
- Remove precipitating cause
- Improve functional status of the patient

Non-pharmacologic

- Give oxygen if the infant or child is showing signs of respiratory distress.
- Avoid the use of intravenous fluids whenever possible.
- Support the child in a semi – sitting position with hand and shoulders elevated and lower limbs dependent.
- Relieve fever with paracetamol to reduce the cardiac workload.
- Avoid added salt diets make sure the child gets adequate nutrition

PHARMACOLOGIC

A. Diuretics

First line

- **Furosemide,** 1mg/kg, intravenously and wait for marked diuresis within 2 hours. If not effective, give 2mg/kg and repeat in 12 hours, if necessary. Then a single dose of 1 – 2mg/kg P.O. is usually sufficient. If furosemide is given for more than 5 days, or if it is given with digoxin, potassium supplementation is necessary.

Alternative

- **Spironolactone**, 2 – 3mg/kg/24 hours in two to three divided dose *PLUS*
- **Hydrochlorothiazide** 2mg/kg/24hr, (maximum dose 100mg/24hr) in two divided doses**.**

B. Positive inotropic medicines

These are used when the cause of Heart Failure is due to decreased contractility

- **Digoxin**, 15 micrograms/kg P.O. loading dose followed by 5 micrograms/kg after 12 hours starting the loading dose and the same dose after 24 hours. Give maintenance dose of digoxin 5micrograms/kg/day.

HEART FAILURE, MAINTENANCE THERAPY

Pharmacologic

A. Diuretics

First line

- ○ **Furosemide,** single dose of 1 – 2mg/kg P.O. is usually sufficient. If furosemide is given for more than 5 days, or if it is given with digoxin, potassium supplementation is necessary.

Alternative

- **Spironolactone**, 2 – 3mg/kg/24 hours in two to three divided doses *PLUS*
- **Hydrochlorothiazide** 2mg/kg/24hr, (maximum dose 100mg/24hr) in two divided doses**.**

B. Positive inotropic medicines

These are used when the cause of Heart Failure is due to decreased contractility

- **Digoxin**, 5 micrograms/kg after 12 hours starting the loading dose and the same dose after 24 hours. Give maintenance dose of digoxin 5micrograms/kg/day.

FOLLOW UP

- Follow-up is mandatory

FURTHER READING

1. Nigussie B, Tadele H. Heart failure in Ethiopian children: Mirroring the unmet cardiac services. Ethiopian Journal of Health Sciences. 2019;29(
2. Yadeta D, Hailu A, Haileamlak A, Gedlu E, Guteta S, Tefera E, Tigabu Z, Tesfaye H, Daniel W, Mekonnen D, Zelalem M. Prevalence of rheumatic heart disease among school children in Ethiopia: A multisite echocardiography-based screening. International journal of cardiology. 2016 Oct 15;221:260-3.

16.7.5 HYPERTENSION IN CHILDREN

BRIEF DESCRIPTION

- **Normal BP**: records of less than or equal to 90th percentile for age, gender and height is considered to be normal
- **Elevated BP**: records of greater than 90th or less than 95th percentile for age, gender and height is considered to be prehypertension.
- **Stage I hypertension**: BP records that lie between 95th percentile and 5mmHg above the 99th percentile for age, gender and height.
- **Stage 2 hypertension**: BP records that lie that exceeds 5mmHg above the 99th percentile for age, gender and height.

PRIMARY HYPERTENSION

- The most common reason for high blood pressure is the inherited (genetic) form known as primary hypertension.
- This accounts for the majority of cases with hypertension.
- The cause of primary hypertension is unknown.

- Children and adolescents with primary hypertension are often overweight.

SECONDARY HYPERTENSION:

- Renal parenchymal disease (GN, HUS, congenital anomalies, obstructive UP) and renovascular diseases account for about 90% of secondary hypertension in children.
- Other causes include cardiovascular disorders, endocrinpathies, CNS disorders,

CLINICAL FEATURES

- Hypertension is known as a silent killer because it usually has no signs and symptoms.
- Most patients with hypertension feel fine and do not know that their blood pressure is elevated.
- When hypertension is very severe or advanced, symptoms may include headache, fainting and loss of kidney function.
- In late stages, convulsions may occur.

TREATMENT

Objectives

- Prevent complication of Hypertension
- Improve functional status of the patient

Note: Children do not usually suffer the life-threatening cardiovascular effects of high blood pressure. The negative effects of hypertension usually develop over many years. Finding it early allows us to find the appropriate ways to address it and lower the blood pressure.

Non-Pharmacologic

- If blood pressure is high, measuring it again is important. If the blood pressure remains high, we recommend the following changes:
  - Achieving proper weight through diet and exercise for patients who are overweight

  - Cutting down on salt in the diet
- Limit sodium content

Pharmacologic

- Many antihypertensive drugs are available for the treatment of chronic hypertension. The choice of drug is usually based on the mode of action and the potential for adverse effects.
- Refer to specialist.

FURTHER READING

1. Falkner B. Hypertension in children and adolescents: epidemiology and natural history. Pediatric nephrology. 2010 Jul 1;25(7):1219-24.
2. Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. Jama. 2007 Aug 22;298(8):874-9.

16.8 ENDOCRINE DISORDERS IN CHILDREN

16.8.1 DIABETES MELLITUS

BRIEF DESCRIPTION

- Diabetes mellitus describes a group of disorders, which are phenotypically characterized by persistently high blood glucose levels.

CAUSES

- Type 1: decreased insulin production due to autoimmune destruction of the pancreas. Usually starts at a young age
- Type 2: insulin resistance usually combined with insufficient production of insulin as the disease progresses. Usually starts in adulthood
- Secondary diabetes: due to other identifiable causes, e.g., Cushing's syndrome, chronic pancreatitis, etc.

RISK FACTORS

- Type 1: genetic factors, environmental factors (e.g., some viral infections)
- Type 2: family history, unhealthy diet, obesity, lack of exercise, smoking

CLINICAL FEATURES

- Large amounts of urine (polyuria)
- Thirst and excessive drinking of water (polyuria)
- Unexplained weight loss (especially in type 1)
- Blurred vision
- Recurrent skin infections
- Recurrent itching of the vulva
- Symptoms related to chronic complications
- Abnormal sensory / motor neurologic findings on extremities
- Foot abnormalities (various deformities, ulcers, ischemia)
- Visual impairment

Note: Type 2 diabetes often only presents with minor a specific symptom, and it is diagnosed either by screening or when the patient presents with complications.

Investigations

- Newly diagnosed patient
    - Fasting or random blood glucose
    - Urine ketones
    - Urine protein
    - Blood urea, electrolytes and creatinine
    - Fasting lipid profile

Note: In the absence of severe hyperglycemia, the diagnosis of Diabetes Mellitus should be confirmed with repeat fasting blood sugar determination.

CURRENT DIAGNOSTIC CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS:

- Fasting plasma glucose (FPG) ≥126 mg/dl
- Hemoglobin A1C ≥6.5%
- A random plasma glucose ≥200 mg/dl, in patients with classic symptoms of hyperglycemia or hyperglycemic crisis
- Two-hour plasma glucose ≥200 mg/dl during an oral glucose oral tolerance test after 75gm anhydrous glucose dissolved in water of glucose

Note: In the absence of unequivocal hyperglycemia (very high levels of blood sugar), criteria 1-3 should be confirmed by repeated testing. One single slightly elevated blood sugar in the absence of symptoms IS NOT DIAGNOSTIC for diabetes.

COMPLICATIONS

- Acute coma due to diabetic ketoacidosis, or hyperosmolar hyperglycemia (see next section), or hypoglycemia
- Stroke, ischemic heart disease, kidney failure
- Blindness, impotence, peripheral neuropathy
- Diabetic foot which may lead to amputations

Differential diagnosis

- Diabetes insipidus, HIV/AIDS, TB

TYPE 1 DIABETES

Treatment of Type 1 Diabetes Mellitus

Objectives

- Relieve symptoms
- Prevent acute hyperglycemic complications

- Prevent chronic complications of diabetes
- Prevent treatment-related hypoglycemia
- Achieve and maintain appropriate glycemic targets
- Ensure weight reduction in overweight and obese individuals

Non-pharmacologic

- **Medical Nutrition Therapy (MNT)**
    - Avoid refined sugars as in soft drinks, or adding to their teas/other drinks.
    - Be encouraged to have complex carbohydrates.
        - Low in animal fat.
        - Increase in the amount of fiber e.g., vegetables, fruits and cereals
- **Exercise**
    - Regular moderate-intensity aerobic physical activity for at least 30 minutes at least 5 days a week or at least 150 min/week.
    - Encouraged to resistance training three times per week for type -2 diabetes
- **Self-blood glucose monitoring (SBGM)**
- **Screening and treatment of micro and macro vascular complications**

Pharmacologic

- Mixed insulin (70% NPH insulin + 30% regular insulin)
- The dose of starting insulin depends on the age of the patient and whether the patient has presented with DKA or not.
    - **Initiation** - 0.2 to 0.4units/ kg/ day twice daily injection**-** before breakfast and before supper
    - **Maintenance – highly variable** roughly 0.6 to 0.7 units/kg/day

Table 16. 14. Properties of common insulin preparations and insulin analogues

Preparation	**Onset (hr.)**	**Peak(hr.)**	**Effective Duration(hr.)**
Short acting			
Regular (more intermediate than short acting)	0.5–1.0	2–3	4–6
Long acting			
NPH	1–4	6–10	10–16
Mixed			
70/30 = 70% NPH + 30% regular	0.5–1.0	Dual peak (as regular + as NPH)	10 -16

DIABETIC KETOACIDOSIS

- Acute metabolic complications of diabetes mellitus: DKA is characterized by ketosis, acidosis, and hyperglycemia. It is more common in type I diabetes.

RISK FACTORS

- Newly diagnosed diabetes
- Loss of diabetic control resulting in significant glucosuria, ketonuria and volume depletion.
- May be initiated by intercurrent illness, stress,
- Missed insulin.

CLINICAL FEATURES

- Acute onset:
  - Polyuria, polydipsia, polyphagia, weight loss
  - Emesis, abdominal pain, fruity breath

  - Labored respirations (deep breathing, acidotic)
  - Dehydration, hypotension
  - Sweet, acetone smell on the breath (from Ketones)
  - Altered mental status - stupor, coma
- Free water losses exceed salt depletion.
- Hyperglycemia (-1.6 mEq NA+/1 per change 100mg/dl glucose)
- Usual ANION GAP is 20-30 mEq/L: (Na-Cl-CO2)

DIFFERENTIAL DIAGNOSIS

- Other causes of ketoacidosis/hyperglycemia
- Other causes of acute abdominal pain
- Other causes of coma

INVESTIGATIONS

- Blood sugar
- Urine analysis (for ketones, positive)
- Full blood count
- Renal function and electrolytes (Na, K)

TREATMENT OBJECTIVES

- Relieve symptoms
- Prevent acute hyperglycemic complications
- Achieve and maintain appropriate glycemic targets

TREATMENT

- Brief history, physical examination, and assessment of mental status and degree of dehydration. Accurate weight.
- Use diabetic flow sheet to document fluids, insulin, and lab results.
- **First hour:**
  - IV fluids: normal saline - 20 ml/kg bolus over the first hour

- Regular Insulin after one hour of rehydration 0.05-0.1 units/kg/hr if continuous IV infusion if not first dose of insulin 0.5u/kg/d give ½ IM and ½ IV, Subsequent doses should be 0.5u/kg/d SC every 4-6 hours. Dose adjustment in case of a rapid fall in RBS>100mg/dl, and hypokalemia that has persisted despite administration of K+ by ½
- NPO until substantial clinical improvement is seen
- Nasogastric tube and Foley catheter for (1) shock or (2) stupor/coma
- Maintain accurate Intake and Output.
- Cardiac monitor if K+ abnormal or pH <7.20.
- Mannitol at bedside for severe DKA

- **Second hour**
  - Repeat glucose and electrolytes one hour after insulin and IV fluids initiated. Continue hourly glucose and electrolytes until patient is ready for discharge or admission.
  - Fluid/Insulin

Table 16. 15. Fluid and insulin administration in diabetic ketoacidosis

	pH >7.25 and TCO_2>15	pH <7.25 and/pr TCO_2<15
Fluids	PO fluids. If emesis: follow guidelines for pH <7.25	**A. IV rate:** • Patients initially presenting to ED • [(85 cc/kg + maint) - bolus]23 • Patients given IV fluids prior to treatment in ED [(85 cc/kg + maint) - IV fluids prior to arrival] 24 - # of hours of IV fluid administration prior to arrival • Slow rehydration is the current recommendation **B. Fluid** • BG >250: 0.45 NS with 20 mEq/L K phosphate and 20 mEq/L K acetate • BG <250: RBS <250MG/DL change fluid type to 0.45%NS with D5W

	pH >7.25 and TCO_2>15	pH <7.25 and/pr TCO_2<15
Insulin	SQ Insulin	• 0.1 units/kg/hr IV continuous infusion until pH and electrolytes corrected. • Adjust insulin dose to lower blood glucose no greater than 100 mg/dl/hr and to stabilize at 150-200 mg/dl. • The insulin infusion can be lowered by 50-75% if needed.

- **Third hour**
  - Repeat electrolytes (as necessary), glucose, and pH
  - Continue Fluid/Insulin recommendations as per second hour.
- Adjunctive therapy.
  - Close observation of mental status is critical. The potential for cerebral edema in severe DKA is significant (2%). For sudden CNS deterioration give Mannitol I g/kg IV bolus.
  - Bicarbonate administration is rarely indicated. Please consult an endocrinologist prior to its use.
- Discharge home if:
  - Bicarbonate >15 and pH >7.30 and po tolerated.
  - For new diabetic-eligibility criteria must be met, endocrinologist notified, and follow-up arranged.
  - Indications to temporarily stop insulin infusions during DKA therapy: uncontrolled hypoglycemia severe

Hypokalemia

- Treatment for Hypokalemia (K < 3.5mEq/l)
- Attempt IV 0.5-1.0 mEq/kg of K-lyteor
- If unable to tolerate PO, increase IV K+ to 60-80 mEq/L and maintain the same IV rate.

be alert for these signs and any Central nervous system deterioration:

- Any decrease in serum Na with therapy: SIADH?
- Any deterioration of alertness or orientation; headache or "fussy" behavior.
- Onset of stupor or coma. Development of Babinski reflex or hyperreflexia.
- Decrease or lack of continuous improvement in pH or bicarbonate after first hour of fluid therapy (may need to increase insulin drip)

PREVENTION

- Early detection
- Good control of diabetes
- Prompt treatment of infections
- General education

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HYPOGLYCEMIA IN DIABETIC CHILDREN

- A clinical condition due to reduced levels of blood sugar (glucose). Symptoms generally occur with a blood glucose <3.0 mmol/L (54mg/dl).

CAUSES

- Overdose of insulin or anti-diabetic medicines
- Sepsis, critical illnesses
- Hepatic disease

- Starvation
- Tumors of the pancreas (insulinomas)
- Certain drugs e.g., quinine
- Hormone deficiencies (cortisol, growth hormone)

CLINICAL FEATURES

- Early symptoms: hunger, dizziness, tremors, sweating, nervousness and confusion
- Profuse sweating, palpitations, weakness
- Convulsions
- Loss of consciousness

DIFFERENTIAL DIAGNOSIS

- Other causes of loss of consciousness (poisoning, head injury etc.)

INVESTIGATIONS

- Blood sugar (generally <3.0 mmol/L)
- Specific investigations: to exclude other causes of hypoglycemia

TREATMENT

Objectives

- Relieve symptoms
- Prevent acute hypoglycemic complications
- Achieve and maintain appropriate glycemic targets

Non-pharmacologic

- If patient is able to swallow
- Oral glucose or sugar 10-20 g in 100-200 ml water (2-4 teaspoons) is usually taken initially and repeated after 15 minutes if necessary

PHARMACOLOGIC

- If patient is unconscious: Dextrose 10% IV 2-5 ml/kg If patient does not regain consciousness after 30 minutes, consider other causes of coma
- Monitor blood sugar for several hours (at least 12 if hypoglycemia caused by oral antidiabetics) and investigate the cause – manage accordingly

Note

- After dextrose 50%, flush the IV line to avoid sclerosis of the vein (dextrose is very irritant)
- Preparation of Dextrose 10% from Dextrose 5% and Dextrose 50%:
- Remove 50 ml from Dextrose 5% bottle and discard
- Replace with 50 ml of Dextrose 50%. Shake
- Follow normal aseptic techniques
- Use immediately, DO NOT STORE

PREVENTION

- Educate patients at risk of hypoglycemia on recognition of early symptoms e.g., diabetics
- Advise patients at risk to have regular meals and to always have glucose or sugar with them for emergency treatment of hypoglycemia
- Advise diabetic patients to carry an identification tag

FURTHER READING

- Kahsay H, Fantahun B, Nedi T, Demoz GT. Evaluation of Hypoglycemia and Associated Factors among Patients with Type 1 Diabetes on Follow-Up Care at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia. Journal of diabetes research. 2019 Apr 10;2019.
- Tsadik AG, Gidey MT, Assefa BT, Abraha HN, Kassa TD, Atey TM, Feyissa M. Insulin injection practices among youngsters with diabetes in Tikur Anbesa Specialized Hospital, Ethiopia. Journal of Diabetes & Metabolic Disorders. 2020 Jun 16:1-8.

TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS

Treatment of Type-2 Diabetes Mellitus

Non-pharmacologic

- Medical Nutrition Therapy (MNT)
    - Avoid refined sugars as in soft drinks, or adding to their teas/other drinks.
    - Be encouraged to have complex carbohydrates.
        - Low in animal fat.
        - Increase in the amount of fiber e.g., vegetables, fruits and cereals
- Exercise
    - Regular moderate-intensity aerobic physical activity for at least 30 minutes at least 5 days a week or at least 150 min/week.
    - Encouraged to resistance training three times per week for type -2 diabetes
- Self-blood glucose monitoring (SBGM)
- Screening and treatment of micro and macro vascular complications

Table 16. 16. Glycemic Targets for Children

Fasting plasma glucose (capillary)	**70-130 mg/dl**
Postprandial (1–2 h after the beginning of the meal) plasma glucose	**< 180 mg/dl**
Hemoglobin A1C	**< 7%**

Pharmacologic

- Oral blood glucose lowering drugs

Metformin

- It is the first line drug for initiation of therapy

- If intolerant to metformin or have a contraindication to it, sulfonylureas can be the initial drugs to start treatment.
- **Metformin**, 500 mg, p.o.daily with meals. Titrate dose slowly depending on blood glucose levels or HbA1C to a maximum dose 2000 -2500mg
- **ADRs**: abdominal discomfort and diarrhea, lactic acidosis
- **C/Is**: Serum creatinine >1.5 mg/dL (men) >1.4 mg/dL (women), CHF, radiographic Iodinated contrast studies, seriously ill patients, acidosis, hepatic failure
- If blood sugar targets are not achieved - Option of referral for patients who fail to respond to metformin

ADD

- **Sulfonylureas**
    - **Glibenclamide**, 2.5 mg -5mg, p.o.daily 30 minutes before breakfast
    - Titrate dose slowly depending on HbA1c and/or fasting blood glucose levels to 15 mg daily.
    - When 7.5 mg per day is needed, divide the total daily dose into 2, with the larger dose in the morning.
    - Avoid in patients with renal impairment.

N.B- **If postprandial hyperglycemia remains high with good fasting blood sugar while patient is on basal insulin regimen as depicted above; pre meal short acting agents can be added.**

- **If poorly controlled with the above treatment, refer for further therapy**

MANAGEMENT OF OTHER CARDIOVASCULAR RISKS

- Aspirin, 75–162 mg, p.o, once/day
    - Indications:
        - Increased cardiovascular risk (10-year risk >10%)

    - Men >50 years of age or women >60 years of age who have at least one additional major risk factor (Hypertension, Smoking, Dyslipidemia, Albuminuria and family history of CVD)

- Antihypertensive (See treatment of hypertension)
    - ACE inhibitors or ARBS are the drugs of choice
- **Prevention of Type-2 Diabetes Mellitus**

FURTHER READING

1. Nadeau K, Dabelea D. Epidemiology of type 2 diabetes in children and adolescents. Endocrine research. 2008 Jan 1;33(1-2):35-58.
2. Tekalegn Y, Addissie A, Kebede T, Ayele W. Magnitude of glycemic control and its associated factors among patients with type 2 diabetes at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. PloS one. 2018 Mar 5;13(3):e0193442.

16.8.2 OBESITY IN CHILDREN AND ADOLESCENTS

BRIEF DESCRIPTION

- Overweight and obesity are an abnormal or excessive fat accumulation that presents a risk to health.
- It is a risk factor for many diseases and is linked to many deaths.
- Body mass index (BMI) is a simple index of weight-for-height used to classify overweight and obesity.

BMI = Weight (in kilograms)

Height (in meters) squared (m2)

Table 16. 17. In children, age needs to be considered when defining overweight and obesity

CLASSIFICATION	CRITERIA
Underweight	BMI < -2 Z score
Healthy body weight	BMI 18 to 25 Adolescents
Overweight	WFH >2 Z score WHO Child Growth Standards median
Obesity	WFH >3 Z score WHO Child Growth Standards median

CAUSES

- High energy (i.e., calorie) intake: eating too much, eating a lot of fatty food
- Low expenditure of energy: sedentary lifestyle, no exercise or limited activity
- Disease: hypothyroidism, diabetes mellitus, pituitary cancer

RAISED BMI IS A MAJOR RISK FACTOR FOR:

- Cardiovascular disease: heart disease and stroke
- Diabetes mellitus
- Musculoskeletal disorders: osteoarthritis
- Some cancers: endometrial, breast, ovarian, prostate, liver, kidney, gallbladder, kidney
- Obstructive sleep apnoea
- Fatty liver, gallstones

CLINICAL FEATURES

- Overweight, difficulty breathing, poor sleeping patterns
- Joint damage due to weight, low fertility

- Poor self-image, antisocial, depression
- In children, also increased risk of fractures, hypertension, cardiovascular disease, insulin resistance

INVESTIGATION

- Blood pressure, blood glucose, cholesterol

TREATMENT

Objectives

- Prevent complications
- Ensure weight reduction in overweight and obese individuals

Non-pharmacologic

- Advise patient to reduce carbohydrate and fat intake and increase fruit, fiber and vegetable intake
- Refer patient to a nutritionist for individualized diet counseling, and to compile a diet plan
- Advise patient to control appetite, participate in hobbies, treat any depression
- Advise patient to increase physical activity and exercise daily.
- Advise to start slowly and build up gradually
- Warn the patient of their high risk of diabetes, heart disease, hypertension, stroke, and general poor health
- Encourage patient not to give up even when the weight loss process is slow

PREVENTION AND HEALTH EDUCATION

- Limit energy intake from total fats and sugars: reduce fatty meat, palm cooking oil (replace with sunflower, olive, corn oil)
- Increase consumption of fruits and vegetables, as well as legumes, whole grains and nuts

- Engage in regular physical activity (60 minutes a day for children and 150 minutes spread through the week for adolescent)

FURTHER READING

- Gebrie A, Alebel A, Zegeye A, Tesfaye B, Ferede A. Prevalence and associated factors of overweight/obesity among children and adolescents in Ethiopia: a systematic review and meta-analysis. BMC obesity. 2018 Dec;5(1):19.
- Tadesse Y, Derso T, Alene KA, Wassie MM. Prevalence and factors associated with overweight and obesity among private kindergarten school children in Bahirdar Town, Northwest Ethiopia: cross-sectional study. BMC research notes. 2017 Dec 1;10(1):22.

16.8.3 THYROID DISEASES

1. HYPOTHYROIDISM

BRIEF DESCRIPTION

- A condition resulting from thyroid hormone deficiency.
- It is 5 times more common in females than in males.

CAUSES IN CHILDREN:

A. Primary hypothyroidism

- Defect in thyroid gland development:
- Dyshormonogenesis
- Defect in TSH- receptor responsiveness
- Iodine deficiency/endemic goiter
- TG synthesis defect
- Hypofunctioning gland: autoimmune diseases, radioactive iodine, drugs, surgical removal

B. Secondary hypothyroidism:

- Cause is central

CLINICAL FEATURES

- Dull facial expression, puffiness, periorbital swelling
- Hoarse voice, slow speech
- Weight gain, drooping eyelids
- Hair sparse, coarse, and dry: skin dry, scaly, and thick
- Forgetfulness, other signs of mental impairment
- Gradual personality change
- Bradycardia, constipation (often), anemia (often)
- Paresthesia (numbness) of hands and feet

INVESTIGATIONS

- Blood levels of thyroid hormone (low T3, T4, high TSH)
- Levothyroxine => Child: refer for specialist management
- Once stable, check hormone levels every 6-12 months

DIFFERENTIAL DIAGNOSIS

- Myasthenia gravis
- Depression

TREATMENT

- Pharmacologic treatment: levothyroxine 25-50microgram daily dose

Note: In most cases, the treatment is for life

Prevention

- Educate patients on the use of iodized salt

FURTHER READING

1. Bona G, Prodam F, Monzani A. Subclinical hypothyroidism in children: natural history and when to treat. Journal of clinical research in pediatric endocrinology. 2013 Mar;5(Suppl 1):23.
2. Monzani A, Prodam F, Rapa A, Moia S, Agarla V, Bellone S, Bona G. Endocrine disorders in childhood and adolescence. Natural history of subclinical hypothyroidism in children and adolescents and potential effects of replacement therapy: a review. European Journal of Endocrinology. 2013 Jan;168(1): R1-1.

2. THYROTOXICOSIS

BRIEF DESCRIPTION

- Excess thyroid hormone in the blood results in thyrotoxicosis.
- If left untreated, significant weight loss and cardiac complications, including heart failure, may occur.
- The major causes are toxic multi-nodular goiter, Grave's disease and hyper functioning solitary adenoma

CLINICAL FEATURES

- Weight loss despite increased appetite, Excessive sweating, Heat intolerance
- Tremors, Nervousness and irritability, Tremors, Moist palms
- Menstrual irregularity and sub-fertility
- Staring or protruding eyes
- Heart failure, Rapid pulse rate which may be irregular
- Goitre often present but not always
- Smooth and diffuse goitre in Grave's disease
- Irregular goitre in toxic multi-nodular goiter

INVESTIGATIONS AND TREATMENT:

- If suspected clinically refer for investigation and management.

16.9 GASTROINTESTINAL DISORDERS

16.9.1 GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN (GERD)

BRIEF DESCRIPTION

- Dyspepsia with mainly heart burn caused by regurgitation of gastric contents into the lower esophagus (acid reflux).

PREDISPOSING FACTORS

- Hiatus hernia
- Increased intra-abdominal pressure
- Gastric ulcer

CLINICAL FEATURES

Young children may have effortless vomiting

- Heartburn: a burning sensation in the chest.
    - Usually brought about by bending or exertion or lying down
- Unpleasant sour taste (due to stomach acid reflux)
- Oesophagitis with pain and difficulty when swallowing
- Halitosis, bloating and belching
- Nausea, chronic pharyngitis

COMPLICATIONS

- Dysphagia
- Reflux asthma

DIFFERENTIAL DIAGNOSIS

- Peptic ulcer, gastritis, pancreatitis

Investigations

- Gastroscopy
- Barium meal and follow through
- Therapeutic trial before invasive investigations

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Modify diet: avoid precipitating causes and, thickening of the formula or feeds
- Avoid feeding in semi erect position

Pharmacologic

- Antacid suspension: Magnesium trisilicate compound 1-2 tablets every 8 hours
- If no response and no alarm signs: Omeprazole 5-10kg ➔5mg po daily, 10-20kg= 10mg daily, >20kg ➔ 20mg po daily once daily for 4 weeks
- If not responding to 4 weeks of omeprazole, refer for further management

FURTHER READING

1. JaruratanasirikulMD S, SriplungMD H.Thyrotoxicosis in children: treatment and outcome. J Med Assoc Thai. 2006;89(7):967-73.

16.9.2 PEPTIC ULCER DISEASE IN CHILDREN

BRIEF DESCRIPTION

- It is ulceration of gastro-duodenal mucosa.
- It tends to be chronic and recurrent if untreated.

CAUSES

- Helicobacter pylori infection
- Drugs (NSAIDS e.g., acetylsalicylic acid, corticosteroids)
- Irregular meals
- Stress
- Alcohol and smoking
- Caffeine-containing beverages

CLINICAL FEATURES

GENERAL

- Epigastric pain typically worse at night and when hungry.
- Vomiting, nausea, regurgitation
- Discomfort on palpation of the upper abdomen
- Bleeding ulcer: Hematemesis (coffee brown or red vomitus), Black stools (i.e., melena)
- Perforated ulcer: Acute abdominal pain, signs of peritonitis such as rigid abdomen, ground coffee-brown vomitus (due to blood)

INVESTIGATIONS AND DIAGNOSIS

- Positive stool antigen for H. pylori.
    - Used for diagnosis and to confirm eradication.
    - This test may give false negative if the patient has been taking antibiotics or omeprazole in the previous 2 weeks
- SERUM ANTIBODY TEST IS NOT USEFUL FOR DIAGNOSIS AND FOLLOW UP
- Gastroscopy, biopsy of stomach wall, barium meal

DIFFERENTIAL DIAGNOSIS

- Pancreatitis, hepatitis
- Disease of aorta, myocardial infarction
- Lung disease (hemoptysis)

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complications

Non-pharmacologic

- Modify diet: avoid precipitating causes and increase milk intake

Pharmacologic

- Give an antacid: Magnesium trisilicate compound 2 tablets every 8 hours as required
- Treatment for eradication of H. pylori (Triple therapy):
    - Combination 1 (First line): Amoxicillin 40mg/kg per dose every 12 hours for 10days PLUS clarithromycin 7.5mg/kg per dose every 12 hours for 10 days PLUS omeprazole 0.5mg/kg per dose every 12 hours for two weeks
- For bleeding and perforated ulcer:
    - Refer patient to hospital immediately for IV fluids and blood if necessary,
    - IV ranitidine 50 mg in 20 ml slowly every 8 hours

Note

- Clarithromycin every 12 hours is preferred instead of metronidazole
- Confirm eradication with stool antigen test a month after completion of treatment; test should be negative

FURTHER READING

1. Taye B, Enquselassie F, Tsegaye A, Amberbir A, Medhin G, Fogarty A, Robinson K, Davey G. Association between infection with Helicobacter pylori and atopy in young Ethiopian children: a longitudinal study. Clinical & Experimental Allergy. 2017 Oct;47(10):1299-308
2. Kitila KT, Sori LM, Desalegn DM, Tullu KD. Burden of Helicobacter pylori infections and associated risk factors among women of child bearing age in Addis Ababa, Ethiopia. International journal of chronic diseases. 2018 Nov 12;2018.

16.9.2 HEPATITIS IN CHILDREN

BRIEF DESCRIPTION

- Hepatitis is an inflammation of the liver with multiple etiologies.
- It presents as an acute illness with jaundice and altered liver function tests or chronically with progressive liver dysfunction.
- When symptoms, signs or laboratory abnormalities persist for more than 6 months it is considered as chronic.
- Common causes include viruses (Hepatitis A, B, C, D and E, EBV etc.), drugs (e.g., anti TB drugs, ARVs, anti-convulsant, paracetamol and herbal medicines), autoimmune disease (autoimmune hepatitis), deposition disease (e.g., Hemochromatosis, Wison's disease)

CLINICAL FEATURES

- Right upper quadrant abdominal pain
- Fever
- Fatigue, malaise, anorexia, nausea and vomiting
- Yellow or dark colored urine and pale stools
- Physical findings include jaundice, right upper quadrant tenderness, hepatomegaly, ascites, edema, astrexis and mental status change

INVESTIGATIONS AND DIAGNOSIS

- AST, ALT, alkaline phosphatase, serum bilirubin, serum albumin, PT or INR
- Hepatitis viral markers - HBSAg, anti HCV antibody, HAV Igm
- Autoimmune markers - ANA
- Abdominal Ultrasound

TREATMENT OF ACUTE HEPATITIS

Objectives

- Identify and treat cause
- Identify and treat precipitants
- Relieve symptoms

Non-pharmacological treatment- treatment of acute hepatitis is mainly supportive

- Withdrawal of hepatoxic drugs or herbal preparation
- Bed rest or hospitalization (if patient has poor oral intake, significant vomiting, signs of encephalopathy)
- High calorie fluids - glucose drinks, fruit juices, light porridge
- Intravenous dextrose (5-10%) infusion – when patient's oral intake is poor or if there is vomiting
- Decrease protein intake- if there is risk of encephalopathy
- Avoid constipation

PHARMACOLOGICAL TREATMENT

- Refer patients with progressive hepatitis to specialist.

REFERENCE

- Tegegne D, Desta K, Tegbaru B, Tilahun T. Seroprevalence and transmission of Hepatitis B virus among delivering women and their new born in selected health facilities, Addis Ababa, Ethiopia: a cross sectional study. BMC research notes. 2014 Dec 1;7(1):239.

16.10 NEUROLOGIC DISEASES IN CHILDREN: SEIZURE DISORDERS AND EPILEPSY

16.10.1 FEBRILE SEIZURES

BRIEF DESCRIPTION

- A generalized tonic-clonic and sometimes focal seizure which is associated with a rapid rise in temperature due to an extracranial illness.
- It is a diagnosis of exclusion: specific conditions (cerebral malaria, meningitis, epilepsy) should be excluded.
- It commonly affects children from age 3 months to 6 years.

CAUSES

- Malaria
- Respiratory tract infections
- Urinary tract infections
- Other febrile conditions

CLINICAL FEATURES

- Elevated temperature (>38 °C)
- Convulsions usually brief and self-limiting (usually <5 minutes, and may be prolonged for more than 15 minutes in complex febrile seizure) but may recur if temperature remains high
- No neurological abnormality in the period between convulsions
- Generally benign and with good prognosis

DIFFERENTIAL DIAGNOSIS

- Epilepsy, brain lesions, meningitis, encephalitis
- Trauma (head injury)

- Hypoglycemia
- If intracranial pathology cannot be clinically excluded (especially in children <2 years) consider lumbar puncture or treat children empirically for meningitis

Investigations

- Blood: Slide/RDT for malaria parasites
- Random blood glucose
- Full blood count
- Urinalysis, culture and sensitivity
- LP and CSF examination
    - Indications for LP:
        - Non-immunized or incomplete immunization
        - Age <6 months
        - Was on antibiotics prior to onset of sz (may mask the clinical signs of meningitis)

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complications

Non-pharmacologic

- Use tepid sponging to help lower temperature

Pharmacologic

- Give an antipyretic: paracetamol 15 mg/kg every 6 hours until fever subsides
- If convulsing: Give diazepam 500 micrograms/kg rectally (using suppositories/rectal tube or diluted parenteral solution) Maximum dose is

10 mg, Repeat prn after 10 minutes

- If unconscious: Position the patient on the side (recovery position) and ensure airways, breathing and circulation (ABC)

PREVENTION

- Educate caregivers on how to control fever (tepid sponging and paracetamol)

FURTHER READING

1. Assogba K, Balaka B, Touglo FA, Apetsè KM, Kombaté D. Febrile seizures in one-five aged infants in tropical practice: Frequency, etiology and outcome of hospitalization. Journal of pediatric neurosciences. 2015 Jan;10(1):9
2. Fetveit A. Assessment of febrile seizures in children. European journal of pediatrics. 2008 Jan 1;167(1):17-27.

16.10.2 STATUS EPILEPTICUS

BRIEF DESCRIPTION

- Status epilepticus generally refers to the occurrence of a single unremitting seizure with duration longer than 5 to 10 minutes or frequent clinical seizures without an interictal return to the baseline clinical state.

INVESTIGATIONS

- Complete blood count, blood culture (in febrile children), serum electrolytes, and blood glucose.
- Blood glucose should also be checked at the bedside and 5 mL/kg 10% dextrose administered if blood glucose is less than 54mg/dl

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complications

NON-PHARMACOLOGIC

- Use tepid sponging to help lower temperature
- Stabilization of the airway, maintenance of adequate ventilation (with oxygen administered as necessary), and circulatory support.
- Intravenous access should then be established as this permits the most rapid delivery of a drug to the brain. If no intravenous access within 3 minutes, then intraosseous access should be established
- The initial laboratory for meningitis and reversible derangements of metabolis

PHARMACOLOGIC

- Dextrose 10% 5mL/kg children
- Diazepam as above in febrile convulsion, repeated after 5-10 min
- If not responsive, Phenytoin 15-18 mg/kg over 1 hour. It is very caustic so use a good IV line. Extravasation will cause tissue damage
- If no response consider Phenobarbital 10-15 mg/kg slowly IV. Dilute the solution with 10 times its volume of water for injections and give VERY SLOWLY (at a rate ≤0.1mg/minute)
- Monitor BP and respiration, be ready to administer IV fluids if hypotension develops and ventilate with Ambu bag in case of respiratory depression Or
- If no response, consider ICU admission.

NOTE

- Diazepam. Intravenous diazepam should be administered over 2 minutes because the risk of respiratory depression is increased with more rapid administration and with more than two doses.
- Rectal diazepam is absorbed rapidly and attains a therapeutic level in 10 minutes
- A longer-acting antiepileptic drug should also be administered because of

the relatively short duration of action of diazepam, Phenytoin is preferred over phenobarbital, which is more likely to cause respiratory depression and to alter the child's level of consciousness.

- In children who are receiving phenytoin prior to the onset of status epilepticus, we recommend the use of a smaller dose

FURTHER READING

1. Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, Jagoda A. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the Guideline Committee of the American Epilepsy Society. Epilepsy currents. 2016 Jan;16(1):48-61
2. Chin RF, Neville BG, Peckham C, et al. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: Prospective population-based study. Lancet 2006;368(9531):222-229.

16.10.2 SEIZURE DISORDERS IN CHILDREN, NON-FEBRILE

BRIEF DESCRIPTION

- A chronic condition characterized by recurrent unprovoked seizures.
- Seizures are caused by abnormal discharges in the brain and present in two different forms: convulsive and non-convulsive forms.
- Consider a diagnosis of epilepsy if:
  - person has had at least 2 unprovoked seizures in the last year calendar.
  - One episode of unprovoked seizure with the following
    - Abnormal neurologic exam
    - Abnormal neuroimaging or EEG finding
    - A diagnosis of epilepsy syndrome

- Seizures during an acute event (e.g., meningitis, acute traumatic brain injury) are not epilepsy.

CAUSES

- Genetic, congenital malformation, birth asphyxia, brain tumour
- Brain infections, cysticercosis, trauma (acute or in the past)
- Metabolic disorders
- In some cases, no specific causes can be identified

CLINICAL FEATURES

- Depending on the type of epilepsy:

A. Generalized epilepsy:

- Seizure involves whole brain, and consciousness is lost at the onset.
- **Tonic Clonic (grand-mal) or convulsive epilepsy**
  - May commence with a warning sensation in the form of sound, light or abdominal pain (aura).
  - There may be a sharp cry followed by loss of consciousness and falling.
  - Tonic contraction (rigidity) of muscles occurs followed by jerking movements (clonic phase)
  - There may be incontinence of urine or faeces, frothing, and tongue biting.
  - A period of deep sleep follows
- **Absence seizures (petit mal)**
  - Mainly a disorder of children
  - The attack is characterized by a brief loss of consciousness (5-10 seconds) in which posture is retained but other activities cease
  - The child has a vacant stare
  - Previous activities are resumed at the end of the attack

  - Several attacks may occur in a single day
- **Atonic or tonic seizures (drop attacks)**
  - Sudden loss of muscular tone, of brief duration (15 seconds), with consciousness maintained or
  - Sudden stiffening of muscle
- **Myoclonus Epilepsy**:
  - Abnormal jerking movements occurring usually in the limbs but may involve the whole body

B. Focal Epilepsy

- Seizure activity starts in one area of the Brain
- **Simple:**
  - Patient remains alert but has abnormal sensory, motor, psychic or autonomic manifestation e.g., jerking of a limb, deja vu, nausea, strange taste or smell, signs of autonomic nerve dysfunction i.e., sweating, flushing, and gastric sensation, motor contraction or sensory change in a particular point of the body)
- **Complex:**

○ Altered awareness and behavior e.g., confusion, repetitive movements

DIFFERENTIAL DIAGNOSIS

- Syncope, hypoglycemia
- Hypocalcemia
- Conversion disorder, hyperventilation and panic attacks

INVESTIGATIONS

- A complete medical assessment including psychiatric history
- Electroencephalogram (EEG)

○ Useful in petit mal and temporal lobe epilepsy

  - To be done at specialist level (RR and NR)
- Other investigations are guided by suspected cause

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complications

Non-pharmacologic

- All suspected cases of non-convulsive epilepsy should be confirmed and treated by a specialist
- Convulsive epilepsy can be diagnosed at hospital/health center level but drug refills should be available at lower level
- One brief isolated seizure does not need further treatment but review at 3 months and re-assess.
- Treat patients with repeated episodes as per definition
- Treatment can effectively control epilepsy in most cases
- Acute seizure and status epilepticus
  - First aid for acute seizure
  - Do not restrain or put anything in the mouth
  - Protect person from injury: make sure they are in a safe place away from fire or other things that might injure them
  - DO NOT leave patient alone.
  - Seek help if possible
  - After the crisis, check airway, breathing and circulation and, while unconscious, put the person in recovery position (on their side)

PHARMACOLOGIC

- Most seizures resolve spontaneously.

- If lasting >3 minutes, give diazepam 10 mg IV or rectal. Child: 0.05 mg/kg rectally, 0.02 mg/kg IV

PHARMACOLOGIC

- Children <2 years: phenobarbital or carbamazepine or phenytoin
- Children >2 years: carbamazepine or valproate
- Absence seizures: Valproate or ethosuximide

PRINCIPLE OF AED THERAPY

- Start with mono therapy. The effective dose must be reached progressively and patient monitored for tolerance and side effects. Aim at the lowest dose able to control (prevent) the seizures
- If treatment is ineffective (less than 50% reduction in crisis) try another monotherapy (slowly reduce the current antiepileptic and introduce the new one)
- If high doses with side effects are required and seizures are anyway infrequent, less than complete control can be the goal
- Follow up monthly until stable, then every 3 months
- Warn patient that treatment interruptions can trigger seizures or even status epilepticus
- If no seizure for 2 years and no known cause like head trauma or infection, consider possibility of stopping treatment (over 2 months). Discuss with the patient
- If 2 mono therapy trials fail, refer to specialist

Note

- In children, look for presence of associated intellectual disability or behavioral problems.
- If present, consider carbamazepine or valproate. (avoid phenobarbital and phenytoin) and manage associated intellectual disability or behavioral problem

HEALTH EDUCATION

- Health education to patients, careers and community
- Advice on management of seizures and safety precautions
- In children, look for and manage presence of associated intellectual disability or behavioral problems

PREVENTION

- Good antenatal care and delivery
- Avoid causative factors

FURTHER READING

1. Friedman MJ, Sharieff GQ. Seizures in children. Pediatric Clinics. 2006 Apr 1;53(2):257-77.
2. Hassen O, Beyene A. The effect of seizure on school attendance among children with epilepsy: a follow-up study at the pediatrics neurology clinic, Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia. BMC Pediatrics. 2020 Dec;20(1):1-7.

16.11 MENTAL HEALTH IN CHILDREN

16.11.1 SEDATION OF AN ACUTELY DISTURBED CHILD OR ADOLESCENT

PRINCIPLE

- A key principle of medical ethics is a child autonomy should be respected
- Physical restraints is only used for safety and/or treatment
- As physical restraints should only be used as last resort
- It should be well coordinated and swift action

ALTERNATIVE MEANS OF CALMING A CHILD

- Crisis prevention: Anticipate and identify early irritable behavior
- Provide a safe containing environment
- Listen and talk simply and in a calm manner
- Offer planned collaborative sedation (ask the child to take some oral medicine)

Indication for restraint

- Other methods Other methods to control the behaviour have failed, such as de-escalation techniques; and
- The child displays aggressive or combative behaviour which arises from a medical or psychiatric condition (including intoxication); and
- The child requires urgent medical or psychiatric care; and
- The behaviour involves a proximate risk of harm to the child or others, or risk of significant destruction of property.

CAUTIONS AND CONTRAINDICATIONS TO PHYSICAL RESTRAINT AND EMERGENCY SEDATION:

- A child who is 'acting out' and who does not need acute medical or psychiatric care should be discharged from the hospital to a safe environment (home, police, DHS) rather than be restrained.
- Be aware of previous medications and possible substance use.
- Safe containment is possible via alternative means (including voluntary, collaborative oral sedation).
- Inadequate personnel/unsafe setting/inadequate equipment.
- Situation judged as too dangerous e.g. the child has a weapon (call a Code Black)

EMERGENCY CHEMICAL RESTRAINT

Procedure

- The Code Grey team should perform this procedure.
- Team leader will designate roles before approaching child.
- All members should **ensure own safety**, with gloves and goggles.
- Draw up medication
- **Secure the child** quickly and calmly using the least possible force. At least five people are required.
- The child should be initially held supine. In highly agitated children, a face down technique may be used at the discretion of the team leader, but be aware of the increased risk of asphyxiation.
- Administer the medications by intramuscular injection into the lateral thigh (other options - ventrogluteal or dorsogluteal). Beware of the risk of needle stick injury. Further titrated doses of medication may be required depending on clinical response (If medication can be given IV this may be an option if the child is safe to cannulate).
- Post sedation care

COMPLICATIONS OF EMERGENCY RESTRAINT

- Complications from medications
- Injury to the child or staff
- Traumatic asphyxiation

COMPLICATIONS OF MECHANICAL RESTRAINTS

- Escape from mechanical restraints
- Pressure effects of mechanical restraints
- Complications of being held supine, such as inability to clear vomitus from airway

ONGOING CARE

- Following restraint, the child must undergo a detailed medical and mental health assessment to guide subsequent management.

- In some cases recommendation and transfer to an inpatient mental health facility may be required (Section 9 of the Victorian Mental Health Act, 1986).
- The need for restraint and sedation should be reviewed on an ongoing basis and the child should be cared for in the least restrictive modality so as to provide safety.
- In most cases, mechanical restraints should be removed once control is gained and this should be done in a stepwise fashion (one limb at a time).
- As the sedation wears off, the child's risk status should be carefully monitored throughout the entire process. Adjuncts to safe care may include the use of the Emergency Behavioural Assessment Room (EBAR), further sedation (oral, IV, IM) or possible use of mechanical restraints.

FURTHER READING

1. Calver LA, Downes MA, Page CB, Bryant JL, Isbister GK. The impact of a standardised intramuscular sedation protocol for acute behavioural disturbance in the emergency department. BMC emergency medicine. 2010 Dec;10(1):1-7.
2. Page CB, Parker LE, Rashford SJ, Isoardi KZ, Isbister GK. A prospective study of the safety and effectiveness of droperidol in children for prehospital acute behavioral disturbance. Prehospital Emergency Care. 2018 Dec 7.

16.11.2 ENURESIS AND ENCOPRESIS

ENURESIS

BRIEF DESCRIPTION

- Enuresis is urinary incontinence after the age at which bladder control is expected.
- It is divided in to two, (primary enuresis; must be at least 5 years old) or after previous normal continence (secondary enuresis).

CLINICAL FEATURES

- It usually presents as bedwetting in the first half of the night (nocturnal enuresis).
- It affects 15% of 5-year-olds, 2% of 10-yearolds and 1% of 14-year-olds.
- Boys outnumber girls 3:1.
- Enuresis can cause great distress, affect self-esteem, interfere with normal activities (e.g. sleepovers) and can lead to bullying or intolerant parenting.

DIAGNOSIS

- In the assessment, exclude urinary tract infection (UTI), diabetes or neurological disorder.
- Enuresis may be a sign of sleep apnoea.
- Search for recent stressors and symptoms of emotional disorder (twice as common as expected in those with enuresis).
- There is often a history of enuresis in male relatives.

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complication

Non-pharmacologic

- Reassurance, explanation and limiting fluid intake in the evening.
- Behavioral methods are the main treatment.
- A star chart is best for younger children;
    - they are rewarded for achieving a realistic target (which may not be a ‘dry bed’ initially) with stars or other suitable token.
- An enuresis alarm (‘pad and buzzer’) is a moisture-sensitive pad worn by the child.

  - When urine is passed, a buzzer goes off, which wakes the child in time to go to the toilet to finish. He or she also participates in changing the sheets.
  - An alarm is usually effective if persisted with for several weeks, especially in children over 7 years old.

Pharmacologic

- These methods are sometimes used, though behavioral methods are preferred.
- Intranasal desmopressin is the usual first-line drug, with moderate success and few side effects.
- The tricyclic antidepressant (TCA) imipramine is licensed for enuresis from the age of 6, but is of limited efficacy, is potentially dangerous and not usually recommended.
- Relapse is common with both methods.

PROGNOSIS

- The prognosis is good, though a few boys remain enuretic into adulthood.

ENCOPRESIS

BRIEF DESCRIPTION

- Encopresis is the passing of faeces in an inappropriate place after age 4.
- As with enuresis, it can be primary or secondary.

CLINICAL FEATURES

- Children may soil their pants, pass faeces in hidden places or occasionally smear them.
- At assessment, exclude physical problems (e.g., constipation, Hirschsprung's disease) and learning disability.

CAUSES

- There is often a history of inadequate or harsh toilet training combined with recent stresses and emotional disorder in the child.

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complication

Non-pharmacologic

- Management is by reassurance; help with associated problems and ensuring that the parents do not become punitive.
- The standard behavioral manoeuvre is to toilet the child after each meal, and to reward her or him for staying there, for producing a motion and for not soiling.

PROGNOSIS

- Most encopresis cases resolve with treatment within a year.
- Occasionally it persists into adolescence.

FURTHER READING

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's pocket handbook of clinical psychiatry. Lippincott Williams & Wilkins; 2010.
2. Gautam Gulati, Mary Ellen Lynall, Kate Saunders: Lecturenotes. Psychiatry—Eleventh edition. John Wiley & Sons, Ltd; 2014

16.11.3 ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

BRIEF DESCRIPTION

- Consists of a persistent pattern of inattention and/or hyperactivity and impulsive behavior that is more severe than expected of children of similar age and level of development.
- Symptoms must be present before the age of 7 years, must be present in at least two settings, and must interfere with the appropriate social, academic, and extracurricular functioning.

- ADHD is often comorbid with conduct disorder, anxiety, depression, tic disorders and pervasive developmental disorders.

CAUSES

- Possible causes include perinatal trauma and genetic and psychosocial factors.
- Evidence of noradrenergic and dopaminergic dysfunction in neurotransmitter systems.
- Frontal lobe hypoperfusion and lower frontal lobe metabolic rates have also been noted.
- Soft neurological signs are found in higher rates among children with ADHD.

EPIDEMIOLOGY

- Occurs in 3% to 7% of grade-schoolers.
- Male-to-female ratio is 3:1 to 5:1.
- Symptoms often present by 3 years.

DIAGNOSIS.

- Principle signs are based on history of child's developmental patterns and direct observation in situations requiring attention. Typical signs include talking excessively, persevering, fidgeting, frequent interruptions, impatience, difficulty organizing and finishing tasks, distractibility, and forgetfulness. Psychiatrist use diagnostic criteria to diagnose ADHD.

DIFFERENTIAL DIAGNOSIS

- Bipolar I disorder. There is more waxing and waning of symptoms.
- Mania. Irritability may be more common than euphoria.
- Learning disorders. Inability to do math or read is not because of inattention.
- Depressive disorder. Distinguished by hypo activity and withdrawal.
- Anxiety disorder. May be manifested by over activity and easy distractibility.

TREATMENT

Objectives

- Alleviate symptoms
- Improve social skills and learning

Non-pharmacologic

- Support and psycho-education for the child and family.
- Specific educational approaches, including attention to associated learning difficulties.
- Firm adherence to behavioural principles (to reward good behaviour and discourage hyperactive behaviour).
- Dietary restriction (e.g., of food additives or colourings) is not generally recommended.

Pharmacologic

- Psychostimulants (e.g., methylphenidate) have an important role.

PROGNOSIS

- ADHD has a variable prognosis. Gradual improvement typically occurs in adolescence, and one-third of cases resolve. The rest have residual hyperkinetic features, especially in those with learning difficulties or conduct disorder. Antisocial personality disorder and substance misuse sometimes develop.

FURTHER READING

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's pocket handbook of clinical psychiatry. Lippincott Williams & Wilkins; 2010
2. Gautam Gulati, Mary Ellen Lynall, Kate Saunders: Lecturenotes. Psychiatry—Eleventh edition. John Wiley & Sons, Ltd; 2014

16.11.4 MOOD DISORDERS IN CHILD AND ADOLESCENCE

BRIEF DESCRIPTION

- Mood disorders can take various forms, from major depressive disorder to less common conditions, such as bipolar disorder and disruptive mood dysregulation disorder.

MAJOR DEPRESSIVE DISORDER

- Major depressive disorder—commonly known as depression—is characterized by chronic feelings of sadness, guilt, or worthlessness.

RISK FACTORS

- A combination of genetic, biological, environmental, and psychological factors causes depression. Stressful situations, such as moving, changing schools, relationship problems, or the death of a loved one, may trigger a depressive episode.
- However, an episode may occur without an obvious trigger. The condition is more common in adolescents than in younger children.

DIAGNOSIS

- A diagnosis of major depressive disorder, or depression, requires that a child experience symptom daily for at least two weeks.
- Symptoms must interfere with the child's daily life. Five of the following symptoms must be present:
    - Low mood or irritability
    - Loss of interest in friends and activities the child had previously enjoyed
    - Changes in appetite
    - Sleep disturbances
    - Loss of energy
    - Slow or agitated movements

- o Feelings of worthlessness or guilt
- o Decreased ability to concentrate
- o Thoughts of suicide or death

PERSISTENT DEPRESSIVE DISORDER

- Several symptoms of persistent depressive disorder overlap with major depressive disorder, though a child with the former has fewer symptoms that are of lower intensity and longer duration for at least a year.

BIPOLAR DISORDER

- A child must have one manic episode, which is characterized by an extended period of excitability or irritability, exaggerated self-confidence, or recklessness.
- Most but not all children and adolescents with bipolar disorder also have intermittent depressive episodes, in which the child has symptoms of depression, such as irritability, persistent sadness, or frequent crying.

DISRUPTIVE MOOD DYSREGULATION DISORDER

- A diagnosis of disruptive mood dysregulation disorder requires that symptoms occur in at least two settings—such as at home and at school—for a year or more. During this period, symptoms must continue without relief for longer than three months at a time.
- Symptoms include three or more temper outbursts per week that are out of proportion to the situation or trigger and are inconsistent with the child's developmental level. The mood between tantrums is persistently irritable.

PROGNOSIS

- A young age of onset and multiple disorders predict a poorer prognosis.
- The mean length of an episode of major depression in children and adolescents is about 9 months.
- Recurrence of a major depressive episode is 40% by 2 years and 70% by 5 years.

- Dysthymic episodes last on average 4 years and are associated with major depression (70%), bipolar disorder (13%), substance abuse (15%), and suicide (12%).

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complication

Non-pharmacologic

- Hospitalization is indicated when a patient is suicidal or has a coexisting substance abuse or dependence.
- Cognitive–behavioral therapy for moderately severe depression aims to challenge maladaptive beliefs and enhance problem-solving abilities and social competence.
- Family education and participation are necessary for depression.
- Modeling and role-playing techniques can be useful in fostering good problem-solving skills.

Pharmacotherapy.

- The SSRIs currently are the drugs of choice in the pharmacological treatment of depressive disorders in children and adolescents.
- Refer to a psychiatrist for better management

FURTHER READING

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's pocket handbook of clinical psychiatry. Lippincott Williams & Wilkins; 2010.
2. Gautam Gulati, Mary Ellen Lynall, Kate Saunders: Lecturenotes. Psychiatry—Eleventh edition. John Wiley & Sons, Ltd; 2014

16.11.5 ANXIETY DISORDERS

BRIEF DESCRIPTION

- Crying when mum goes out, or becoming fearful of spiders, are normal anxieties that children may experience at particular developmental stages, especially at times of stress and transition.
- They must be distinguished from persistent, significant symptoms warranting a diagnosis of anxiety disorder.
- The latter affects 5% of children at some time.
- As in adults, anxiety manifests with behavioral, psychological and physical symptoms.

CLINICAL FEATURES

Behavioral

- Clinging to parent (or other career)
- Unwilling to leave house
- Unwilling to go to bed
- Actions designed to avoid feared event (e.g., hiding)

Psychological

- Feeling worried
- Nightmares

Physical

- Abdominal pain
- Headaches

Separation anxiety

- Among 5–11-year-olds, 3–4% have excessive anxiety when faced with separation from parents or others they are attached to.

  - The child clings to the person and tries to avoid being separated from them.
  - Older children may describe being fearful that the person will be harmed or will not return.
- Sleep disturbance may occur.
- Separation anxiety often begins at times of stress, such as after the death of a loved one or the family pet.
  - Some parents are noted to be overprotective.

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complication

Non-pharmacologic

- Working with the family to explain and reassure.
- Identification and resolution of stressors.
- Ensuring the parents are not reinforcing the problem (e.g. by appearing anxious when about to leave the child).

FURTHER READING

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's pocket handbook of clinical psychiatry. Lippincott Williams & Wilkins; 2010.
2. Gautam Gulati, Mary Ellen Lynall, Kate Saunders: Lecturenotes. Psychiatry—Eleventh edition. John Wiley & Sons, Ltd; 2014

16.11.6 FEEDING AND EATING DISORDERS

BRIEF DESCRIPTION

- Persistent symptoms of inadequate food intake, recurrent regurgitating and rechewing of food, or repeated ingestion of nonnutritive substances.
- Includes pica, rumination disorder, and feeding disorder of infancy or early childhood.

A. PICA.

- Repeated ingestion of a nonnutritive substance for at least 1 month.
- The behavior must be developmentally inappropriate, not culturally sanctioned, and sufficiently severe to merit clinical attention.

DIAGNOSIS.

- Ingestion of nonedible substances after 18 months of age.
- Nonedible includes paint, plaster, string, hair, cloth, dirt, feces, stones, and paper.
- Onset is usually between the ages of 12 and 24 months, and incidences decline with age.
- The clinical implication can be benign or life-threatening depending on objects ingested

EPIDEMIOLOGY

- More common in preadolescents.
- Occurs in up to 15% of those with severe mental retardation.
- Affects both sexes equally.

ETIOLOGY

- Associated with mental retardation, neglect, and nutritional deficiencies (e.g., iron or zinc).
- Onset usually between 1 and 2 years of age.
- Higher-than-expected incidences occur in relatives.

DIFFERENTIAL DIAGNOSIS

- Iron and zinc deficiencies.
- Can occur in conjunction with schizophrenia, autistic disorder, Kleine–Levin syndrome, and anorexia nervosa.

PROGNOSIS.

- Children of normal intelligence remit spontaneously.
- In children, pica usually resolves with increasing age.

TREATMENT

Objectives

- Alleviate symptoms
- Prevent complication

Non-pharmacologic

- In cases of neglect or maltreatment, such circumstances should be altered. Exposure to toxic substances (i.e., lead) should be eliminated.
- Treatments emphasize psychosocial, environmental, behavioral, and family guidance approaches.
- Positive reinforcement, modeling, behavioral shaping, and overcorrection treatment have also been used.

PHARMACOLOGIC

- Mild aversion therapy or negative reinforcement (i.e., a mild electric shock, an unpleasant noise, or an emetic drug) has been successful

B. FEEDING DISORDER OF INFANCY OR EARLY CHILDHOOD.

- Persistent failure to eat adequately for at least 1 month.

EPIDEMIOLOGY

- Occurs in 1.5% of infants, 3% of infants with failure to thrive syndromes, and 50% of infants with feeding disorders.
- Onset is before 6 years of age.

- **Etiology - g**enetic studies indicate a high concordance among monozygotic twins.

DIAGNOSIS

- Failure to eat adequately for at least 1 month in the absence of a general medical or mental condition with a subsequent failure to gain weight or subsequent loss of weight.

DIFFERENTIAL DIAGNOSIS

- Must be differentiated from gastrointestinal structural abnormalities contributing to discomfort during feeding.

PROGNOSIS

- With intervention, failure to thrive may not develop.
- Children with later onset may develop deficits in growth and development when the disorder lasts for several months.
- Seventy percent persistent with the disorder in their first year will continue to have some feeding problems during childhood.

TREATMENT

- Counseling the caregiver is crucial if there are comorbid developmental delays or difficult temperament.
- Cognitive behavioral intervention can be useful.

FURTHER READING

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's pocket handbook of clinical psychiatry. Lippincott Williams & Wilkins; 2010.
2. Gautam Gulati, Mary Ellen Lynall, Kate Saunders: Lecturenotes. Psychiatry—Eleventh edition. John Wiley & Sons, Ltd; 2014

16.11.7 AUTISTIC SPECTRUM DISORDER (ASD)

BRIEF DESCRIPTION

- Autism spectrum disorder (ASD) is a developmental disability that can cause significant social, communication and behavioral challenges.
- A diagnosis of ASD now includes several conditions that used to be diagnosed separately: autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger syndrome.
- Very few autistic children (and adults), called savants, have remarkable abilities in discrete areas, such as complex mental arithmetic (as in the film Rain Man).

CAUSES AND RISK FACTORS

- Most scientists agree that genes are one of the risk factors that can make a person more likely to develop ASD.
- Children who have a sibling with ASD are at a higher risk of also having ASD.
- Individuals with certain genetic or chromosomal conditions, such as fragile X syndrome or tuberous sclerosis, can have a greater chance of having ASD.
- When taken during pregnancy, the prescription drugs valproic acid and thalidomide have been linked with a higher risk of ASD
- There is some evidence that the critical period for developing ASD occurs before, during, and immediately after birth.
- Children born to older parents are at greater risk for having ASD.

CLINICAL FEATURES

- 1 in 100 children from surveys, 80% are boys, Age of onset <3 years. DSM 5 criteria

CORE FEATURES (THE 'AUTISTIC TRIAD')

- Lack social reciprocity ('aloof')
- Impaired language and communication
- Solitary, repetitive behaviours

ASSOCIATED AND COMORBID FEATURES

- Learning disability in 75%, coordination difficulties
- Sensory hypersensitivity or hyposensitivity
- Epilepsy in about 25%, mannerisms and rituals
- Hyperactivity (40%), anxiety, sleep disturbance, hypotonia

DIAGNOSIS

- ASD can sometimes be detected at 18 months or younger.
- By age 2, a diagnosis by an experienced professional can be considered very reliable.
- However, many children do not receive a final diagnosis until much older.
- The diagnosis is made based on a careful history and observations.
- Various checklists and structured interviews are also used.

TREATMENT

Objectives

- Alleviate symptoms
- Improve child development

Non-pharmacologic

- There is currently no cure for ASD.
- However, research shows that early intervention treatment services can improve a child's development.

- Early intervention services help children from birth to 3 years old (36 months) learn important skills.
- Services can include therapy to help the child talk, walk, and interact with others.
- In addition, treatment for particular symptoms, such as speech therapy for language delays, often does not need to wait for a formal ASD diagnosis.
- The main components of management are:
    - Make the diagnosis, and support family in understanding autism and its implications.
    - Consider interventions aimed to improve socialization, communication and behavior.
    - Provide appropriate education and, if required, accommodation.

Pharmacologic

- Deal with associated medical problems (e.g., epilepsy).
- Treat the anxiety.
- Medication is sometimes used, despite very limited evidence. For example, SSRIs for repetitive behaviors, or atypical antipsychotics for severe aggression.

FURTHER READING

1. Sadock BJ, Sadock VA, editors. Kaplan and Sadock's pocket handbook of clinical psychiatry. Lippincott Williams & Wilkins; 2010.
2. Gautam Gulati, Mary Ellen Lynall, Kate Saunders: Lecturenotes. Psychiatry—Eleventh edition. John Wiley & Sons, Ltd; 2014

16.12 CHILDHOOD MALNUTRITION AND GROWTH PROBLEMS

16.12.1 MALNUTRITION

SEVERE ACUTE MALNUTRITION

BRIEF DESCRIPTION

- Malnutrition is a significant contributor to morbidity and mortality among children under 5 years in Ethiopia.
- It also makes the prognosis of other diseases poor.
- The term "malnutrition" commonly refers to under nutrition, and is used as such in these guidelines.
- Although malnutrition can affect all ages, however, the early stages, including, foetus, infants and children, are most vulnerable to the effects of under nutrition during the period of their most rapid physical growth and development during the first two years of life.

CAUSES/CONTRIBUTING FACTORS TO MALNUTRITION

Immediate causes:

- Diet and disease
    - Inadequate quantity and quality of food
    - Lack of knowledge on appropriate foods provided to children, poor food preparation, food taboos
    - Infections: reduce appetite, increase energy and nutrient utilization, and limit the ability to absorb or retain nutrients e.g. in diarrhea, intestinal parasites

ROOT CAUSES:

- Food insecurity, poor health services, poor environmental sanitation, natural disasters, and excessive workload for women,

- poor weaning practices, culture, inadequate water supply, low literacy levels, low nutrition advocacy/education

UNDERLYING CAUSES:

- poverty, corruption, poor governance, poor infrastructure.

CONSEQUENCES OF MALNUTRITION

- Impaired growth, physical and mental and development
- Impaired body resistance/immune system
- Increased risk of adult chronic diseases
- Increased risk of mortality
- Increased risk for the cycle of inter-generational malnutrition
- Poor economic well-being for the individual and country

DIFFERENTIAL DIAGNOSIS

- Nephrotic syndrome (nephritis)
- Liver disease
- Heart disease
- Mal-absorption syndrome
- Malignancy (e.g., gastrointestinal tract cancer, liver cancer/hepatocellular carcinoma)

CLASSIFICATION OF MALNUTRITION

Acute

- Is an indicator of current nutritional status, reflecting recent weight changes or disruption in nutrient intake
- Most appropriate indicator to use in an emergency setting (e.g. due to sudden/sharp period of food shortage)
- Associated with loss of body fat and severe wasting

- Children are thinner than their comparable age group of same height
- Classified as Moderate or Severe based on anthropometry (measurement of the size, weight and proportions of the human body), biochemistry and clinical assessment

CHRONIC

- Is an indicator of the nutritional status overtime; chronically malnourished children are shorter (stunted) than their comparable age group

CLINICAL FEATURES OF MALNUTRITION

- Non edematous **(Marasmus)**:
  - Severe wasting, old man's face, excess skin' hangs around the buttocks, ribs and zygoma bones are prominent, scapular blades and extremities (limbs), eyes are sunken
  - Apathetic or irritable, appetite is fairly good, skin is almost normal, hair demonstrates some changes but not as dramatic as in Kwashiorkor, organomegaly is rare (liver and spleen enlargement)
- Edematous (**Kwashiakor)**:
  - Pitting feet oedema, skin desquamation, hair changes, presence of bilateral pitting oedema (oedema of both feet), moon face
  - Appears adequately nourished due to excess extra cellular fluid, but is very miserable, apathetic
  - Skin changes (dermatosis, flaky paint dermatitis)
  - Hair changes: Silky, straight, sparsely distributed; easily, painlessly pluck able
  - Severe pallor of the conjunctiva, mucous membranes, palms, and soles, loss of skin turgor (dehydration)
  - Organomegaly (liver, spleen) is common
- **Marasmus-kwashiakor**:
  - Most common form,

- ○ presents with features of both Marasmus and Kwashiorkor

Table 16. 18. Diagnostic criteria for malnutrition

Age	• Criteria
Moderate Acute Malnutrition	• WFH/L between -3 and -2 z-scores • Or MUAC 115 up to 125 mm Or low weight for age
Severe Acute Malnutrition 6 months to 18 years	**Without complications** • Oedema of both feet (kwashiorkor with or without severe wasting) OR • WFH/L less than -3 z scores OR • MUAC less than 115 mm OR • Visible severe wasting AND • able to finish RUTF **With complications** • Oedema of both feet OR • WFH/L less than -3 z scores OR • MUAC less than 115 mm OR • Visible severe wasting AND • Any one of the following: • Medical complication present OR • Not able to finish RUTF

Infants < 6 months or <3kg	• The infant is too weak or feeble to suckle effectively (irrespective of his/her weight-for-length, weight-for-age or other anthropometry) or • The infant is not gaining weight at home (by serial measurement of weight during growth monitoring, i.e. change in weight-for-age) or • W/L (Weight-for-Length) less than <-3 Z-score, or • Presence of bilateral pitting oedema.

**The aim of treatment of these patients is to return them to full exclusive breastfeeding. Thus, the admission criterion is failure of effective breastfeeding and the discharge criterion is gaining weight on breast milk alone (anthropometry is not used as primary admission criterion).*

INVESTIGATIONS

- Children with SAM should always be first assessed with a full clinical examination to confirm presence of any danger sign, medical complications, and tested for appetite.
- Assess patient's history of:
    - o Recent intake of food, loss of appetite, breastfeeding
    - o Usual diet before current illness
    - o Duration, frequency and type of diarrhea and vomiting
    - o Family circumstances: Cough >2 weeks and contact with TB, Contact with measles
    - o Known or suspected HIV infection/exposure
- Initial examination for danger signs and medical complications:

    A. Shock: lethargy or unconscious, cold hands, slow capillary refill (<3 seconds), weak pulse, low blood pressure

B. Signs of dehydration, Severe palmar pallor, Bilateral pitting oedema, Eye signs of vitamin A deficiency: dry conjunctiva, corneal, ulceration, keratomalacia, photophobia

C. Local signs of infection: ear, throat, skin, pneumonia, Signs of HIV

D. Fever (≥37.5) or hypothermia (rectal temp <35.5)

E. Mouth ulcers

F. Skin changes of kwashiorkor: hypo- or hyperpigmentation, desquamation, ulcerations all over the body, exudative lesions (resembling burns) with secondary infection (including candida)

LABORATORY TESTS

- Blood glucose
- Complete blood count or Hgb, malaria, HIV, electrolytes
- Stool microscopy for ova and cysts, occult blood, and parasites
- Chest X-ray: Look for evidence of tuberculosis or other chest abnormalities
- Conduct an appetite test:
    - Assess all children ≥6 months for appetite at the initial visit and at every follow up visit to the health facility
- Determine WFH/L:
    - Measure the child's height and weight and plot the score on the appropriate chart (boy or girl).
    - Match the value to the z-score on the right y-axis to determine the child's z-score.
- Measure MUAC:
    - Using a MUAC tape, measure the circumference of the child's upper arm and plot the score on the appropriate chart (boy or girl.
    - Please note: 1 cm=10 mm, so 11.5 cm = 115 mm.

TREATMENT

- For details in the management of severe malnutrition in this group of infants, the reader is advised to refer to the Integrated Management of Newborn and Childhood illnesses, WHO, 2011.

OBJECTIVE

- Treat life-threatening complications
- Rehabilitate with nutrition
- Achieve catch-up growth

GENERAL PRINCIPLES OF MANAGEMENT

- Admit all children with any danger sign, medical complications, pitting oedema or those who fail appetite tests for inpatient care and treatment for complicated SAM.
- Keep them in a warm area separated from infectious children, or in a special nutrition area.
- Children with good appetite and no medical complications can be managed as outpatients for uncomplicated SAM.
- Grade + and ++ edema can be admitted to OTP center if the following holds true: without medical complication, with MUAC >11.5cmWHL/H> 3 Z score
- Adequate facilities and staff to ensure correct preparation of therapeutic foods, and to feed child regularly day and night, should be available.
- Accurate weighing machines and MUAC tapes should be available
- Proper records of feeds given and child's measurements should be kept so that progress can be monitored
- Explain to patient/care-giver to handle the child gently

Table 16. 19. Criteria for admission to in-patient or outpatient care

Factor	Inpatient care	Outpatient care
Anthropometry	6 months to 18 yrs.: • W/H or W/L <70% OR • MUAC <110mm with length >65cm • MUAC <180mm with recent weight loss or underlying chronic illness OR • MUAC<170mm OR • BMI <16	
Bilateral pitting edema	• Bilateral pitting edema grade 3(+++) • Marasmic – kwashiorkor	• Bilateral pitting edema Grade 1 to 2 (+ and++)
Appetite	• Poor appetite	• Good appetite
Choice of caregiver	• Chooses to start, continue or transfer to inpatient treatment • No suitable or willing caregiver	• Chooses to start, continue transfer to outpatient treatment reasonable home circumstance and a willing caregiver
Skin	• Open skin lesions	• No open skin lesions

MODERATE ACUTE MALNUTRITION

DIAGNOSTIC CRITERIA

- WFH/L between -3 and -2 z-scores Or MUAC 115 up to 125 mm OR low weight for age

TREATMENT OF MODERATE MALNUTRITION

- Assess the child's feeding and counsel the mother on the feeding recommendations
- If child has any feeding problem, counsel and follow-up in 7 days
- Assess for possible TB infection.
- Advice mother when to return immediately (danger signs)

FOLLOW-UP CARE

- Follow-up in 30 days
- Reassess child and re-classify
- If better, praise mother and counsel on nutrition.
- If still moderate malnutrition, counsel and follow up in 1 month.
- If worse, losing weight, or feeding problem: Admit/refer

MANAGEMENT OF SEVERE ACUTE MALNUTRITION

- Management involves three phases: initial stabilization for 1 week, transition and rehabilitation (for weeks 2-6).
- Prevent hypo glycaemia by giving small sips of sugar water, keep the child warm, first dose of antibiotics (ampicillin + gentamicin).
- Triage the children to fast-track seriously ill patients for assessment and care: treat shock, hypo glycaemia, and corneal ulceration, immediately.

PHASE I (INPATIENT FACILITY)

- Poor appetite and/or major medical complications.
- Formula used during this phase is F75.

- Weight gain at this stage is dangerous.

TRANSITION PHASE

- Avoid a sudden change to large amount of diet before physiological function is restored.
- Patients start to gain weight as F100 is introduced.
- The quantity of F100 given is equal to the quantity of F75 given in phase I.

PHASE II (REHABILITATION)

- Good appetite
- No major medical complications
- Can occur at inpatient or outpatient setting
- F100 (inpatient only) or ready to use therapeutic feeding (RUTF).

TREATMENT OF COMPLICATIONS

Dehydration

- "Therapeutic window" is narrow in a patient with severe acute malnutrition
- Quickly go from having depleted circulation to over-hydration with fluid overload and cardiac failure
- IV infusions should be avoided whenever possible except in case of shock.
- The standard protocol for the well-nourished dehydrated child should not be used.
- A supply of modified ORS or ReSoMal should never be freely available for the caretakers to give to the child whenever there is a loose stool.

A. NON-EDEMATOUS (MARASMIC) PATIENT

- The usual signs of dehydration are not reliable.
- History is more important than physical examination.
- A definite history of significant recent fluid loss – usually diarrhea, which is clearly like, water (not just soft or mucus) and frequent with sudden onset

within the past few hours or days.

- History of a recent change in the child's appearance.
- If the eyes are sunken then the mother must say that the eyes have changed to become sunken since the diarrhea has started.
- The child must not have any edema.
- Shock may be diagnosed when there is definite dehydration plus a weak or absent radial or femoral pulse, and cold hands and feet, and decrease in level of consciousness.

TREATMENT

- Rehydration should be **oral** whenever possible.
    - IV infusions should be avoided except when there is shock or loss of consciousness from confirmed dehydration
- Weight is the best measurement of fluid balance.
- Before starting any rehydration treatment, weigh the child; mark the edge of the liver and the skin with indelible pen and record respiratory rate.
- Start with 5ml/kg of Rehydration salt for malnourished (ReSoMal), every 30 minutes for the first 2 hours orally or by NG – tube and then adjust according to the weight change observed.
    - If continued weight loss, increase the rate of administration of ReSoMal by 10ml/kg/hr.
    - Weigh child every hour and assess liver size, respiration rate, and pulse rate and pulse volume.
- **Note**: Be alert for signs of over hydration: dangerous and can lead to heart failure.
    - Check for:
    - Weight gain (make sure it is not quick or excessive).
    - If increase in pulse rate by 25/minute, respiratory rate by 5/minute is present, stop ReSoMal.

- Reassess after 1 hour:
    - ✓ Urine frequency (if child urinated since last check),
    - ✓ Enlarging liver size on palpation,
    - ✓ frequency of stools and vomit
- To make ReSoMal half strength (45 mmol Na/L) from the new 75 mmol Na/L WHO-ORS, add 1.7 L of cooled boiled water to each 1-litre sachet of WHO-ORS, add 33ml electrolyte mineral solution and 40g sugar.

B. KWASH PATIENT

- All children with edema have an increased total body water and sodium.
    - They are over -hydrated.
- Edematous patients cannot be dehydrated although they are frequently Hypovolemic.
- If a child with kwashiorkor has definite watery diarrhea and the child is deteriorating clinically (excessive weight loss, more than 2% of the body weight per day), then the fluid lost can be replaced on the basis of 30ml of ReSoMal per day.

SEPTIC SHOCK

- A fast weak pulse with cold extremities
- Disturbed consciousness
- Give broad – spectrum antibiotics
- Keep warm to prevent or treat hypothermia
- Give sugar – water by mouth or nasogastric tube as soon as the diagnosis is made.
- Full blown septic shock – treat as in the Marasmic patient.
- Treat hypothermia, severe anemia, severe pneumonia and any major medical complication

PREVENTION

- Same as in dehydration in well-nourished child, except that ReSoMal is used instead of standard ORS. Give 30-50 ml of ReSoMal (for child <2 years) and 100 ml (for child ≥2 years) after each watery stool

FURTHER READING

1. World Health Organization. Guideline: updates on the management of severe acute malnutrition in infants and children. World Health Organization; 2013.
2. Trehan I, Goldbach HS, LaGrone LN, Meuli GJ, Wang RJ, Maleta KM, Manary MJ. Research Article (New England Journal of Medicine) Antibiotics as part of the management of severe acute malnutrition. Malawi Medical Journal. 2016;28(3):123-30.

16.12.2 GROWTH PROBLEMS

BRIEF DESCRIPTION

- A growth delay occurs when a child isn't growing at the normal rate for their age.
- The delay may be caused by an underlying health condition, such as growth hormone deficiency or hypothyroidism.
- In some cases, early treatment can help a child reach a normal or near-normal height.

CLINICAL FEATURES

- If height is smaller than 95 percent of child age, and the rate of growth is slow.
- A growth delay may also be diagnosed in a child whose height is in the normal range, but whose rate of growth has slowed.
- Depending on the underlying cause of their growth delay, there may be other symptoms:
    - o Arms or legs may be out of normal proportion to the torso.

  - Low levels of the hormone thyroxine, loss of energy, constipation, dry skin, dry hair, and trouble staying warm.
  - Low levels of growth hormone (GH), it can affect the growth of the face, causing the child to look abnormally young.
  - Delayed growth is caused by stomach or bowel disease, there may be blood in the stool, diarrhea, constipation, vomiting, or nausea.

CAUSE

- **A family history of short stature**: The child may be shorter than average simply because of genetics.
- **Constitutional growth delay**: Children with this condition are shorter than average but grow at a normal rate. They usually have a delayed "bone age," meaning their bones mature at a slower rate than their age. They also tend to reach puberty later than their peers. This leads to a below average height in early teenage years, but they tend to catch up with their peers in adulthood.
- **Growth hormone deficiency**: Children with a partial or complete GH deficiency won't be able to sustain a healthy rate of growth.
- **Hypothyroidism:** Babies or children with hypothyroidism have an underactive thyroid gland. The thyroid is responsible for releasing hormones that promote normal growth, so delayed growth is a possible sign of an underactive thyroid.
- **Turner syndrome**: It is a genetic condition that affects females who are missing a part or all of one X chromosome. While children with TS produce normal amounts of Growth Hormone, their bodies don't use it effectively.

OTHER CAUSES OF DELAYED GROWTH

- Less common causes of delayed growth include:
  - Down syndrome, a genetic condition in which individuals have 47 chromosomes instead of the usual 46

  - Skeletal dysplasia, a group of conditions that cause problems with bone growth
  - Certain types of anemia, such as sickle cell anemia
  - Kidney, heart, digestive, or lung diseases
  - Use of certain drugs by the birth mother during pregnancy
  - Poor nutrition
  - Severe stress

DIAGNOSIS

- Child's personal and family health history, including:
  - The birth mother's pregnancy
  - The child's length and weight at birth
  - The heights of other people in their family
  - Information about other family members who have experienced growth delays

Physical examination: chart of the child's growth for six months or more.

- Certain tests and imaging studies can also help for the diagnosis.
- A hand and wrist X-ray can provide important information about the child's bone development in relationship to the age.
- Blood tests can identify problems with hormone imbalances or help detect certain diseases of the stomach, bowel, kidney, or bones.
- Advanced test like GH, chromosomal test for Down syndrome or TS.

TREATMENT

Objectives

- Ensure proper physical growth of the child
- Avoid long term complications of bone deformity

Non-pharmacologic

- It depends on the cause of the delayed growth.
- No treatment or intervention for a family history or constitutional delay,
- For other underlying causes, the following treatments or interventions may help them start growing normally.

PHARMACOLOGIC

- For treatment for Growth hormone deficiency, Hypothyroidism, Turner syndrome and the like the patient need to be referred to specialist

PROGNOSIS

- It depends on the cause of the growth delay and time of treatment.
- If their condition is diagnosed and treated early, they may reach normal or near-normal height.
- Waiting too long to start treatment can raise the risk of short stature and other complications.

FURTHER READING

1. Mesman J, Stoel R, Bakermans-Kranenburg MJ, van IJzendoorn MH, Juffer F, Koot HM, Alink LR. Predicting growth curves of early childhood externalizing problems: Differential susceptibility of children with difficult temperament. Journal of Abnormal Child Psychology. 2009 Jul 1;37(5):625.
2. Sultan M, Afzal M, Qureshi SM, Aziz S, Lutfullah M, Khan SA, Iqbal M, Maqsood SU, Sadiq N, Farid N. Etiology of short stature in children. J Coll Physicians Surg Pak. 2008 Aug 1;18(8):493-7.

16.12.3 VITAMIN A DEFICIENCY

BRIEF DESCRIPTION

- Vitamin A is required for growth, health and proper functioning of surface tissues, including the epithelium of skin, mucus membranes, ocular tissues, particularly the cornea, conjunctiva and retina.

- Vitamin A is found naturally in dark-green leafy and yellow vegetables, tubers, and fruits; and occurs (preformed) in eggs, milk, liver, and fish.
- Children with vitamin A are likely to suffer from systemic illnesses, including diarrhea, pneumonia, and measles.

CLINICAL FEATURES

- Night blindness or nyctalopia
- Thinning and lightening of hair,
- Weight loss,
- Dry and scaling of skin.

CLASSIFICATION OF XEROPHTHALMIA

- $\mathbf{X_N}$ - Night blindness
- $\mathbf{X_{1A}}$ - Conjunctival xcrosis
- $\mathbf{X_{1B}}$ - Bitot's spots
- $\mathbf{X_2}$ - corneal xerosis
- $\mathbf{X_{3A}}$- Corneal ulceration/keratomalasia involving less than one third of the corneal surface
- $\mathbf{X_{3B}}$- Corneal ulceration/keratomalasia involving one third or more of the corneal surface
- $\mathbf{X_S}$- Corneal scars presumed secondary to xerophthalmia
- $\mathbf{X_F}$ - Xerophthalmic fundus

INVESTIGATIONS

- Nutritional history and clinical findings

TREATMENT

Objectives

- Correct vitamin A deficiency

- Prevent blindness in patients with measles and malnutrition

NON-PHARMACOLOGIC

Both for treatment and prevention

- Dietary, economic and social factors
- Breast feeding up to the age of 2 years
- Adequate fat, protein in the diet
- Nutritional: dark-green leafy vegetables, yellow vegetables, fruits, milk, eggs

PHARMACOLOGIC:

- Vitamin A in different doses based on the objective of treatment

I. XEROPHTHALMIA TREATMENT SCHEDULE FOR CHILDREN OVER ONE YEAR AND UNDER 6 YEARS OLD

- Immediately on diagnosis: 200,000 IU vitamin A P.O.
- Following day: 200,000 IU vitamin A P.O.
- Four weeks later: 200,000 IU vitamin A P.O.
- N.B. If there is persistent vomiting or profuse diarrhea, 100,000 IU (water soluble) vitamin

II. DISEASES-TARGETED PREVENTION SCHEDULE FOR PRESCHOOL CHILDREN AT HIGH RISK*

- Children over 1 year and under 6 years old 200,000 IU vitamin A P.O. at first contact with a health care worker for each episode of illness
- Infants under 1 year old and children 100,000 IU vitamin A P.O. at first contact of any age who weigh less than 8 kg a health care worker for each episode of illness

*Those presenting with measles, severe PEM, acute or prolonged diarrhea, acute lower respiratory infections.

III. UNIVERSAL - DISTRIBUTION PREVENTION SCHEDULE FOR PRESCHOOL CHILDREN AND LACTATION MOTHERS

- Children over 1 year and under 6 years 200,000 IU vitamin A P.O. every 3-4 months old who weigh 8 kg or more
- Children over 1 year and under 6 years 200,000 IU vitamin A P.O. every 3-4 months old who weigh less than 8 kg
- Infants 100,000 IU vitamin A P.O. at 6 months*
- Lactating mothers 200,000 IU vitamin A P.O. at delivery or during the next 2 months; this will raise the concentration of vitamin A in the breast milk and help to protect the breast-fed infant

*Best treatment protocol: 25,000IU orally at each of the three PENTA visits, the polio immunization, and then at 9 months (measles immunization).

ADRs: irritability

Refer: In severe and complicated cases refer to an ophthalmologist

FURTHER READING

1. Sahile Z, Yilma D, Tezera R, Bezu T, Haileselassie W, Seifu B, Ali JH. Prevalence of Vitamin A Deficiency among Preschool Children in Ethiopia: A Systematic Review and Meta-Analysis. BioMed Research International. 2020 Mar 4;2020.
2. Demissie T, Ali A, Mekonen Y, Haider J, Umeta M. Magnitude and distribution of vitamin A deficiency in Ethiopia. Food and nutrition bulletin. 2010 Jun;31(2):234-41.

16.12.4 VITAMIN C DEFICIENCY (SCURVY)

BRIEF DESCRIPTION

- Vitamin C plays a role in collagen, carnitine, hormone, and amino acid formation.
- It is essential for bone and blood vessel health and wound healing and facilitates recovery from burns.

- It is also an anti-oxidant, supports immune function, and facilitates the absorption of iron.
- Dietary sources of vitamin C include citrus fruits, tomatoes, potatoes, broccoli, strawberries, and sweet peppers.
- Severe vitamin C deficiency results in scurvy, a disorder characterized by hemorrhagic manifestations and abnormal osteoid and dentin formation.

CAUSE

- Inadequate diet
- The need for dietary vitamin C is increased by febrile illnesses, inflammatory disorders (particularly diarrheal disorders), cold or heat stress, surgery, burn, and protein deficiency.
- Heat (eg, sterilization of formulas, cooking) can destroy some of the vitamin C in food.

CLINICAL FEATURES

- Lassitude, weakness, irritability, weight loss, and vague myalgias and arthralgias may develop early.
- Symptoms of scurvy (related to defects in connective tissues) develop after a few months of deficiency.
    - Follicular hyperkeratosis, coiled hair, and perifollicular hemorrhages may develop.
    - Gums may become swollen, purple, spongy, and friable; they bleed easily in severe deficiency.
    - Eventually, teeth become loose and avulsed. Secondary infections may develop.
    - Wounds heal poorly and tear easily, and spontaneous hemorrhages may occur, especially as ecchymoses in the skin of the lower limbs or as bulbar conjunctival hemorrhage.
- Other symptoms and signs include femoral neuropathy due to hemorrhage into femoral sheaths (which may mimic deep venous thrombosis), lower

extremity edema, and painful bleeding or effusions within joints.

- In infants, symptoms include irritability, pain during movement, anorexia, and slowed growth. In infants and children, bone growth is impaired, and bleeding and anemia may occur.

DIAGNOSIS

- Diagnosis of vitamin C deficiency is usually made clinically in a patient who has skin or gingival signs and is at risk of vitamin C deficiency.
- Laboratory confirmation may be available.
    - Complete blood count is done, often detecting anemia.
    - Bleeding, coagulation, and prothrombin times are normal.
- Skeletal x-rays can help diagnose childhood (but not adult) scurvy.
    - Changes are most evident at the ends of long bones, particularly at the knee.
    - Early changes resemble atrophy. Loss of trabeculae results in a ground-glass appearance.
    - The cortex thins. A line of calcified, irregular cartilage (white line of Fraenkel) may be visible at the metaphysis.
    - A zone of rarefaction or a linear fracture proximal and parallel to the white line may be visible as only a triangular defect at the bone's lateral margin but is specific.
    - The epiphysis may be compressed. Healing subperiosteal hemorrhages may elevate and calcify the periosteum.
- If available laboratory diagnosis, which requires measuring blood ascorbic acid, is sometimes done at academic centers.
    - Levels of < 0.6 mg/dL (< 34 mcmol/L) are considered marginal;
    - Levels of < 0.2 mg/dL (< 11 mcmol/L) indicate vitamin C deficiency.
- **If available determine** Serum B12 value in children

TREATMENT

Objectives

- Correct vitamin C deficiency
- Prevent acute and long-term complication

Non-Pharmacologic

- Nutritious diet with supplemental ascorbic acid

Pharmacologic

- In scurvy, therapeutic doses of ascorbic acid restore the functions of vitamin C in a few days. The symptoms and signs usually disappear over 1 to 2 weeks. Chronic gingivitis with extensive subcutaneous hemorrhage persists longer.

PREVENTION

- Most fruits and vegetables (recommended daily) provide > 200 mg of vitamin C.

FURTHER READING

1. Kittisakmontri K, Swangtrakul N, Padungmaneesub W, Charoenkwan P. Gingival bleeding and bloody dialysate: a case report of scurvy in a child with end-stage renal disease receiving peritoneal dialysis. Journal of Renal Nutrition. 2016 Nov 1;26(6):407-11.

2. Herrador Z, Sordo L, Gadisa E, Buño A, Gómez-Rioja R, Iturzaeta JM, de Armas LF, Benito A, Aseffa A, Moreno J, Cañavate C. Micronutrient deficiencies and related factors in school-aged children in Ethiopia: a cross-sectional study in Libo Kemkem and Fogera districts, Amhara Regional State. PloS one. 2014 Dec 29;9(12):e112858.

16.12.5 VITAMIN D DEFICIENCY (RICKETS)

BRIEF DESCRIPTION

- Rickets is a disease caused by deficiency of vitamin D.

- It is a condition in which there is failure to mineralize growing bone or osteoid tissue.
- The early changes of rickets are seen radiographically at the ends of long bones, but evidence of demineralization in the shafts is also present.
- If rickets is not treated at this stage, clinical manifestations appear.

CAUSE

- Rickets can result from either inadequate intake of vitamin D caused by inadequate direct exposure to sunlight, the rays of which do not pass-through ordinary window glass or inadequate vitamin D intake, or both.
- Rickets usually appears toward the end of the first and during the second year of life.

CLINICAL FEATURES

- Craniotabes: one of the earliest clinical signs of rickets caused by thinning of the outer table of the skull (ping-pong ball sensation when pressing firmly over the occiput or posterior parietal bones).
- Box like appearance of the head (caput quadratum)
- Delayed teeth eruption
- Palpable enlargement of the costochondral junctions (rachitic rosaries)
- Thickening of the wrists (wrist widening)
- Thickening of the ankles (double malleoli)
- Pigeon breast deformity (projecting forward of the sternum)
- A horizontal depression along the lower boarder of the chest (Harrison's groove)
- Bowing of the legs (genu varum deformity) or knock-knees (genu valgum deformity), are relatively late signs occurring after the child starts to bear weight.
- Deformed pelvis and retardation of linear growth

- Greenstick fractures (late signs)

INVESTIGATIONS

- X-ray of the wrist: Decreased bone density, cupping and fraying at the ends of the long bones (best appreciated at the distal end of the radius and ulna) and widened joint space (best appreciated at the wrist joint)
- Normal or low serum calcium, low serum phosphate and high serum alkaline phosphatase, and high serum parathormone levels

TREATMENT

Objectives

- Ensure proper physical growth of the child
- Avoid long term complications of bone deformity
- Avoid acute complications, including recurrent pneumonia, hypocalcaemia etc.
- Avoid pathological fractures

Non-pharmacologic

- Regular exposure to direct sun light without clothing, without applications of any ointments and no glass windows

Pharmacologic

- Mega dose of Vitamin D (600,000 IU intramuscularly as a single dose)
- Supplement with calcium gluconate or other calcium containing salt to prevent hungry bone syndrome.

PREVENTION

- Regular exposure to direct sun light of infants and young children
- Oral administration of vitamin D especially to those breastfed infants whose mothers are not exposed to adequate sunlight (supplemental dose of 400 IU Vitamin D daily, orally).

FURTHER READING

1. Gebreegziabher T, Stoecker BJ. Vitamin D insufficiency in a sunshine-sufficient area: Southern Ethiopia. Food and nutrition bulletin. 2013 Dec;34(4):429-33.
2. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008 Aug 1;122(2):398-417.

16.13 NEONATAL DISEASES

16.13.1 APNEA, NEONATAL

BRIEF DESCRIPTION

- Apnea is a "pause in breathing of longer than 10 to 15 seconds, often associated with bradycardia, cyanosis, or both.

CAUSE

- The most common cause of apnea in the NICU is apnea of prematurity, but first ALWAYS investigate and rule out the following disorders:

  I. Infection - Sepsis, especially in the first day of life, and nosocomial infections and/or NEC in the first weeks of life

  II. Neurological - Intraventricular hemorrhage, intracranial hemorrhage, neonatal seizures, perinatal asphyxia, or other pathology which could lead to increased intracranial pressure

  III. Cardiovascular - Impairment of oxygenation from congestive heart failure and pulmonary edema (PDA, coarctation, etc.), or from shunting (cyanotic heart disease)

  IV. Pulmonary - Impairment of oxygenation and ventilation from lung disease (surfactant deficiency disease, pneumonia, transient tachypnea of the newborn, meconium aspiration, etc.)

  V. Metabolic - Hypocalcemia, hypoglycemia, hyponatremia or acidosis

VI. Hematological - Anemia

VII. Gastrointestinal - NEC or gastroesophageal reflux

VIII. Temperature regulation - Hypothermia or hyperthermia

VIIII. Drugs - prenatal exposure with transplacental transfer to the neonate of various drugs (narcotics, beta-blockers). Postnatal exposure to sedatives, hypnotics or narcotics.

COMPLICATION

- Apnea in premature infants can result in a failure of the mechanisms that protect cerebral blood flow, resulting in ischemia and eventually leukomalacia.
- During apneic episodes, in an attempt to protect cerebral blood flow cardiac output is diverted away from the mesenteric arteries resulting in intestinal ischemia and possibly necrotizing enterocolitis (NEC).

SURVEILLANCE

- All newborns less than 34 weeks gestational age, or less than 1800 grams birth weight, should be monitored for both apnea and bradycardia.
- If available it is done by applying ECG leads to the chest, which is connected to a bedside respiratory and heart rate monitor.

TREATMENT

Objectives

- Ensure proper physical growth of the neonate
- Avoid acute complications, including leukomalacia necrotizing enterocolitis (NEC) etc.

Non-pharmacologic

- **Acute**
  - If apneic, pale, cyanotic or bradycardic, then **tactile stimulation** needs to be given.

  - If the infant does not respond, **bag and mask ventilation**, along with suctioning and airway positioning, may be needed.

- **CHRONIC**
  - The management of apnea of prematurity always involves diagnosing and correcting other potential etiologies, before attributing a specific neonate's apnea to prematurity alone.

PHARMACOLOGIC THERAPY

- Methylxanthines - the most common drugs used to treat apnea:
- Caffeine citrate (1,3,7-trimethylxanthine)
- Better to refer the infant to Neonatal ICU.

FURTHER READING

1. Mengesha HG, Sahle BW. Cause of neonatal deaths in Northern Ethiopia: a prospective cohort study. BMC public health. 2017 Dec 1;17(1):62.
2. Alebel A, Wagnew F, Petrucka P, Tesema C, Moges NA, Ketema DB, Melkamu MW, Hibstie YT, Temesgen B, Bitew ZW, Tadesse AA. Neonatal mortality in the neonatal intensive care unit of Debre Markos referral hospital, Northwest Ethiopia: a prospective cohort study. BMC pediatrics. 2020 Dec;20(1):1-1.

16.13.2 ENTEROCOLITIS, NECROTIZING

BRIEF DESCRIPTION

- Necrotizing enterocolitis (NEC, a bowel infection) may occur in low-birth-weight babies, especially after enteral feeds are started.
- It is more common in low-birth-weight babies fed artificial formulae, but may occur in breastfed babies.

CLINICAL PRESENTATIONS

- Common signs of NEC are:
  - Abdominal distension or tenderness

  - Intolerance of feeding
  - Bile-stained vomit or bile-stained fluid up the nasogastric tube
  - Blood in the stools
- General signs of systemic upset include
  - Apnoeas
  - Drowsy or unconscious
  - Fever or hypothermia

Investigation

- Take a supine and lateral decubitus abdominal X-ray.
  - If there is gas in the abdominal cavity outside the bowel there may be a bowel perforation.
  - Presence of pneumatosis intestinalis is diagnostic of NEC

DIAGNOSIS

- Clinical

TREATMENT

Objective

- Treat life-threatening complications
- Rehabilitate with nutrition
- Achieve catch-up growth

Non-pharmacologic

- Stop enteral feeds.
- Pass a nasogastric tube and leave it on free drainage.
- Examine the baby carefully each day.
- Reintroduce expressed breast milk feeds by nasogastric tube when the abdomen is soft and not tender, the baby is passing normal stools with no

blood and is not having bilious vomiting.

- Start feeds slowly and increase slowly by 1–2 ml per feed each day.
- Surgery if there is perforation

PHARMACOLOGIC

- Start an IV infusion of glucose/saline
- Start antibiotics: give ampicillin (or penicillin) plus gentamicin plus metronidazole for 10 days.
- If the baby has apnoea or other danger signs,
    - Give oxygen by nasal catheter.
    - If apnoea continues give aminophylline or caffeine IV.
- If the baby is pale,
    - Check the haemoglobin and transfuse if Hb<10 g/dL.
    - Ask a surgeon to see the baby urgently.

FURTHER READING

1. Alsaied A, Islam N, Thalib L. Global incidence of Necrotizing Enterocolitis: a systematic review and Meta-analysis. BMC pediatrics. 2020 Dec;20(1):1-5.
2. Sawh SC, Deshpande S, Jansen S, Reynaert CJ, Jones PM. Prevention of necrotizing enterocolitis with probiotics: a systematic review and meta-analysis. PeerJ. 2016 Oct 5;4:e2429.

16.13.3 HEMORRHAGIC DISEASE OF THE NEWBORN

BRIEF DESCRIPTION

- Hemorrhagic disease is a bleeding problem that occurs in a baby during the first few days of life.
- Babies are normally born with low levels of vitamin K, an essential factor in blood clotting.

- A deficiency in vitamin K is the main cause of hemorrhagic disease in newborn babies.

EPIDEMIOLOGY

- Vitamin K deficiency results in bleeding in less than 2 percent of all babies.
- Babies at risk for developing hemorrhagic disease are:
    - Babies who don't receive preventive vitamin K in an injection at birth
    - Exclusively breastfed babies (breast milk contains less vitamin K than cow's milk formula)
    - Babies whose mothers take anti-convulsant medications

CLINICAL FEATURES

- Symptoms may include:
    - Blood in your baby's bowel movements
    - Blood in urine
    - Oozing around the umbilical cord

DIAGNOSIS

- In addition to a complete medical history and physical examination, a diagnosis is based on the signs of bleeding and by laboratory tests for blood clotting times.

TREATMENT/PREVENTION

- Administration of intramuscular (IM) vitamin K is of primary importance in the medical care of neonates.
- A single dose of IM vitamin K after birth effectively prevents classic vitamin K deficiency bleeding.

COMPLICATION

- Without the clotting factor, bleeding occurs, and severe bleeding or hemorrhage can result

16.13.4 HYPOGLYCEMIA, NEONATAL

BRIEF DESCRIPTION

- Neonatal hypoglycemia, defined as a plasma glucose level of less than 45 mg/dL (2.5 mmol/L).
- It is the most common metabolic problem in newborns.

CLINICAL FEATURES

- Infants in the first or second day of life may be asymptomatic or may have life-threatening central nervous system (CNS) and cardiopulmonary disturbances.
- Symptoms can include the following:
  - Hypotonia, lethargy, apathy, poor feeding
  - Jitteriness, seizures
  - Congestive heart failure, cyanosis, apnea, hypothermia
- Clinical manifestations associated with activation of the autonomic nervous system include the following:
  - Anxiety, tremulousness
  - Diaphoresis, tachycardia, pallor
  - Hunger, nausea, and vomiting
- Clinical manifestations of hypoglycorrhachia or neuroglycopenia include the following:
  - Headache
  - Mental confusion, staring, behavioral changes, difficulty concentrating
  - Visual disturbances (eg, decreased acuity, diplopia)
  - Dysarthria, seizures
  - Ataxia, somnolence, coma

DIAGNOSIS

- Serum or plasma glucose levels
- Urine: Obtain a first-voided urine dipstick for ketones; send urine for organic acid analysis
- Screening for metabolic errors if it is available

COMPLICATION

- Major long-term sequelae include neurologic damage resulting in mental retardation, recurrent seizure activity, developmental delay, and personality disorders. Some evidence suggests that severe hypoglycemia may impair cardiovascular function.

TREATMENT

Objective

- Treat life-threatening complications
- Rehabilitate with nutrition

Non-pharmacologic

- Hypoglycemia should be treated as soon as possible to prevent complications of neurologic damage.
- Early feeding of the newborn with breast milk or formula is encouraged.
- The mainstay of therapy for children who are alert with intact airway protection includes orange juice at 20 mL/kg.

PHARMACOLOGIC

- For patients who cannot protect their airway or are unable to drink, nasogastric, intramuscular, intraosseous, or intravenous (IV) routes can be employed for the following drugs used to raise glucose levels:
- **Dextrose**, start a 5% or 10% dextrose drip when hypoglycemia is recurrent.

FURTHER READING

1. Agarwal B, Lokeshwar MR. 12.3 Hemorrhagic Disease of the Newborn. Partha's Management Algorithms in Pediatric and Adolescent Practice. 2018 Apr 30:158.
2. Shearer MJ. Vitamin K deficiency bleeding (VKDB) in early infancy. Blood reviews. 2009 Mar 1;23(2):49-59.

16.13.5 JAUNDICE, NEONATAL

BRIEF DESCRIPTION

- More than 50% of normal newborns, and 80% of preterm infants, have some jaundice.
- Jaundice can be divided into Physiologic and pathologic jaundice:

PATHOLOGIC JAUNDICE

- Jaundice started on the first day of life
- Jaundice lasting longer than 14 days in term, 21 days in preterm infants
- Jaundice with fever
- Deep jaundice: palms and soles of the baby deep yellow

PHYSIOLOGICAL JAUNDICE

- Skin and eyes yellow but none of the above

CAUSE

- Abnormal jaundice may be due to
  - Serious bacterial infection
  - Haemolytic disease due to blood group incompatibility or G6PD deficiency
  - Congenital syphilis or other intrauterine infection
  - Liver disease such as hepatitis or biliary atresia

  - Hypothyroidism

INVESTIGATIONS FOR ABNORMAL JAUNDICE

- The clinical impression of jaundice should be confirmed by a bilirubin measurement, where possible.
- The investigations depend on the likely diagnosis and what tests are available, but may include:
  - Haemoglobin or HCT
  - Full blood count to look for signs of serious bacterial infection (high or low neutrophil count with >20% band forms), and to look for signs of haemolysis
  - Blood type of baby and mother, and Coombs test
  - Syphilis serology such as VDRL tests
  - G6PD screen, thyroid function tests, liver ultrasound

TREATMENT

Objective

- Treat life-threatening complications
- Prevent chronic complication

Non-pharmacologic

- Phototherapy if
  - Jaundice on day 1
  - Deep jaundice involving palms and soles of the feet
  - Prematurity and jaundice
  - Jaundice due to haemolysis
- Continue phototherapy until serum bilirubin level is lower than threshold range or until baby is well and there is no jaundice of palms and soles.
- If the bilirubin level is very elevated and Refer for exchange transfusion.

FURTHER READING

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2. Seid SS, Ibro SA, Ahmed AA, Akuma AO, Reta EY, Haso TK, Fata GA. Causes and factors associated with neonatal mortality in neonatal intensive care unit (NICU) of Jimma University medical center, Jimma, south West Ethiopia. Pediatric health, medicine and therapeutics. 2019; 10:39

16.13.6 PREMATURITY/PRETERM NEONATE

BRIEF DESCRIPTION

- Prematurity is a term for the broad category of neonates born at less than 37 weeks' gestation.
- Preterm birth is the leading cause of neonatal mortality and the most common reason for antenatal hospitalization.
- For premature infants born with a weight below 1000 g, the three primary causes of mortality are respiratory failure, infection, and congenital malformation.

CLINICAL FEATURES

- Confirmation of gestational age is based on physical and neurologic characteristics.
- The Ballard Scoring System remains the main tool clinicians use after delivery to confirm gestational age by means of physical examination.

INVESTIGATION AND DIAGNOSIS

- Initial laboratory studies in cases of prematurity are performed to identify issues that, if corrected, improve the patient's outcome.
- Such tests include the following:

  - Frequent blood glucose measurement: This is essential because premature infants are prone to hypoglycemia and hyperglycemia
  - Complete blood count (CBC):Anemia or polycythemia may be revealed that is not clinically apparent
  - White blood cell (WBC) count: A high or low WBC count and numerous immature neutrophil types may be found; an abnormal WBC count may suggest subtle infection
  - Blood type and antibody testing (Coombs test): These studies are performed to detect blood-group incompatibilities between the mother and infant and to identify antibodies against fetal red blood cells (RBCs); such incompatibilities increase the risk for jaundice and kernicterus
  - Serum electrolyte levels: Frequent determination of serum sodium, potassium, calcium, and glucose levels, in conjunction with monitoring of daily weight and urine output in extremely low birth weight (ELBW) infants, assist the clinician in managing fluid and electrolytes
- **IMAGING STUDIES**
  - Chest radiography: to assess lung parenchyma and heart size in newborns with respiratory distress.
  - Cranial ultrasonography: to detect occult intracranial hemorrhage in premature infants.
- **LUMBAR PUNCTURE**
  - Lumbar puncture with blood cultures in those who have clinical signs of central nervous system infection.

TREATMENT

Objectives

- Decrease the risk of grave complications and mortality
- Avoid residual sequelae
- Shorten hospital stay

Non-pharmacologic

- Stabilization in the delivery room with prompt respiratory and thermal management is crucial to the immediate and long-term outcome of premature infants, particularly extremely premature infants.
- Strict monitoring of input and output is crucial.
- Thus, urine output, serum electrolyte levels, and daily weight are critical in handling fluids and electrolytes in premature infants.

RESPIRATORY MANAGEMENT

- Recruitment and maintenance of optimal lung volume in infants with respiratory distress:
  - This step can be accomplished with early use of continuous positive airway pressure (CPAP) given nasally, by nasal mask, or by using an endotracheal tube when mechanical ventilation and/or surfactant is administered
- Avoidance of hyperoxia or hypoxia with the aid of pulse oximetry:
  - Always use blended oxygen with an oxygen saturation target range (SaO 2) of 90-95%.
- Early administration (age <2 hours) of surfactant is recommended when indicated.

THERMOREGULATION

- Use radiant warmers with skin probes to regulate the desired temperature (in general, a normal body temperature of 36.5 °C -37.5°C.
- A heated and humidified isolette is ideal for ELBW infants.

FLUID AND ELECTROLYTE MANAGEMENT

- Preterm infants require close monitoring of their fluid and electrolyte levels for several reasons (eg immature skin increases transepidermal water loss; immature kidney function; the use of radiant warming, phototherapy, mechanical ventilation).

- The degree of prematurity dictates the initial fluid management.
- The following are general principles of fluid and electrolyte management when caring for premature infants:
    - The initial fluid should be a solution of glucose and water
    - Calcium may be added in the initial fluid
    - Iron and vitamin supplementation
    - Screening for ICH…cranial U/S

FURTHER READING

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2. Berhane M, Workineh N, Girma T, Lim R, Lee KJ, Nguyen CD, Neal E, Russell FM. Prevalence of low birth weight and prematurity and associated factors in neonates in Ethiopia: results from a hospital-based observational study. Ethiopian journal of health sciences. 2019;29(6).

16.13.7 RESPIRATORY DISTRESS IN THE NEWBORN

BRIEF DESCRIPTION

- Neonatal respiratory distress syndrome (RDS) is a problem often seen in premature babies.
- Neonatal RDS occurs in infants whose lungs have not yet fully developed.

CAUSES

- The disease is mainly caused by a lack of a slippery substance in the lungs called surfactant.

  - This substance helps the lungs fill with air and keeps the air sacs from deflating.
  - Surfactant is present when the lungs are fully developed.
- Neonatal RDS can also be due to genetic problems with lung development.
- Most cases of RDS occur in babies born before 37 to 39 weeks.
  - The more premature the baby is, the higher the chance of RDS after birth.
  - The problem is uncommon in babies born full-term (after 39 weeks).
- Other factors that can increase the risk of RDS include:
  - Siblings who had RDS
  - Diabetes in the mother
  - Cesarean delivery or induction of labor before the baby is full-term
  - Problems with delivery that reduce blood flow to the baby
  - Multiple pregnancy (twins or more)
  - Rapid labor

CLINICAL FEATURES

- Most of the time, symptoms appear within minutes of birth. However, they may not be seen for several hours.
- Symptoms may include:
  - Bluish color of the skin and mucus membranes (cyanosis)
  - Brief stop in breathing (apnea)
  - Decreased urine output
  - Nasal flaring
  - Rapid breathing
  - Shallow breathing

  - Shortness of breath and grunting sounds while breathing
  - Unusual breathing movement (such as drawing back of the chest muscles with breathing)

INVESTIGATION

- Blood gas analysis -- shows low oxygen and excess acid in the body fluids.
- Chest x-ray -- shows a "ground glass" appearance to the lungs that is typical of the disease. This often develops 6 to 12 hours after birth.
- Lab tests -- help to rule out infection as a cause of breathing problems.

TREATMENT

Objectives

- Decrease the risk of grave complications and mortality
- Shorten hospital stay

Non-pharmacologic

- Babies who are premature or have other conditions that make them at high risk for the problem need to be treated at birth by a medical team that specializes in newborn breathing problems.
- Infants will be given warm, moist oxygen. However, this treatment needs to be monitored carefully to avoid side effects from too much oxygen.
- Having a calm setting, Gentle handling
- Carefully managing fluids and nutrition

Pharmacologic

- A treatment called continuous positive airway pressure (CPAP) may prevent the need for assisted ventilation or surfactant in many babies.
- CPAP sends air into the nose to help keep the airways open. It can be given by a ventilator (while the baby is breathing independently) or with a separate CPAP device.
- Treating infections right away

- Giving extra surfactant to a sick infant has been shown to be helpful.
- Assisted ventilation with a ventilator (breathing machine) can be lifesaving for some babies.

PROGNOSIS

- The condition often gets worse for 2 to 4 days after birth and improves slowly after that. Some infants with severe respiratory distress syndrome will die. This most often occurs between days 2 and 7.
- Long-term complications may develop due to:
  - Too much oxygen.
  - High pressure delivered to the lungs.
  - More severe disease or immaturity. RDS can be associated with inflammation that causes lung or brain damage.
  - Periods when the brain or other organs did not get enough oxygen.

COMPLICATIONS

- Air or gas may build up in:
  - The space surrounding the lungs (pneumothorax)
  - The space in the chest between two lungs (pneumomediastinum)
  - The area between the heart and the thin sac that surrounds the heart (pneumopericardium)
- Other conditions associated with RDS or extreme prematurity may include:
  - Bleeding into the brain
  - Bleeding into the lung (pulmonary hemorrhage; sometimes associated with surfactant use)
  - Problems with lung development and growth
  - Delayed development or intellectual disability associated with brain damage or bleeding

  - o Problems with eye development and blindness

PREVENTION

- Taking steps to prevent premature birth can help prevent neonatal RDS.
- The risk of RDS can also be lessened by the proper timing of delivery.
- A lab test can be done before delivery to check the readiness of the baby's lungs.
- Medicines called corticosteroids can help speed up lung development before a baby is born. They are often given to pregnant women between 24 and 34 weeks of pregnancy who seem likely to deliver in the next week.
- At times, it may be possible to give other medicines to delay labor and delivery until the steroid medicine has time to work.

ALTERNATIVE NAMES

- Hyaline membrane disease (HMD); Infant respiratory distress syndrome; Respiratory distress syndrome in infants; RDS - infants

FURTHER READING

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16.13.8 RESUSCITATION OF THE NEWBORN

BRIEF DESCRIPTION

- For some babies the need for resuscitation may be anticipated:
    - those born to mothers with chronic illness, where the mother had a previous fetal or neonatal death,
    - a mother with pre-eclampsia, in multiple pregnancies,
    - in preterm delivery, in abnormal presentation of the fetus, with a prolapsed cord, or
    - where there is prolonged labor or rupture of membranes, or meconium-stained liquor.
- However, for many babies the need for resuscitation cannot be anticipated before delivery.
- Start resuscitation within one minute of birth if baby is not breathing or is gasping for breath
    - Observe universal hygiene precautions to prevent infection
    - Prepare for resuscitation at each delivery even where there are no signs of foetal distress, just in case the baby requires it

MINIMUM PREPARATION FOR EVERY BIRTH

- Ensure that the following equipment is available and in good working order:

4. Two warm cotton cloths and a small one to position the head
5. Heat source to keep the baby warm
6. Mucus extractor such as a penguin sucker (or bulb syringe)
7. Ambu bag and new-born masks of varying sizes (0 and 1), pulse oximeter
8. Clock or watch
9. A birth attendant skilled in new-born resuscitation

TREATMENT

Objectives

- Decrease complications and mortality
- Prevent sequelae

Non-pharmacologic

- Keep the baby warm by drying the baby using the first cotton cloth and change to the second dry cotton cloth. Rub the back 2-3 times
    - Clamp and cut the cord if necessary
    - Transfer the baby to a dry clean warm surface
    - Tell the mother that the baby is having difficulty starting to breathe and that you will help the baby
- Open the airway
    - Position the head so that it is slightly extended
    - Place a folded towel <2 cm thick under baby's shoulders
    - Suction if secretions in mouth or nose and if baby born through meconium-stained amniotic fluid: suction 5 cm in the mouth, 3 cm in the nose while withdrawing, for max 10 seconds in total.
- Do not suction too deep into the throat as this may cause the heart to slow down or breathing to stop
- If still not breathing, SELECT APPROPRIATE MASK SIZE TO COVER CHIN, MOUTH AND NOSE, AND VENTILATE
    - Form a seal with mask covering chin, mouth and nose
    - Squeeze bag 5 times
    - Observe chest
- If not rising
    - Reposition head, check mask seal, squeeze bag harder

  - Once good seal and chest rising, ventilate for one minute at 40 squeezes per minute then stop and look for breathing
- If breathing >30/minute and no severe chest in drawing
  - Stop ventilating
  - Put baby skin-to-skin on mother's chest
  - Observe every 15 minutes for breathing and warmth:
    - take temperature, count breaths, and observe for chest-in-drawing or grunting respiration.
  - Monitor SpO2
  - Encourage mother to breastfeed within one hour
  - DO NOT LEAVE THE BABY ALONE
- If breathing <30/minute or severe chest in-drawing
  - Continue ventilating
  - Arrange for immediate referral
  - Give oxygen if available
  - Reassess every 1-2 minutes
  - Continue to ventilate during referral
- If not gasping or breathing at all after 20 minutes of ventilation
  - Stop ventilation, the baby is dead

NOTES

- Room air is sufficient in the absence of oxygen
- Cardiac massage is RARELY required; it is dangerous when done incorrectly. A slow heart rate almost always responds to good breathing assistance only
- Usually, there is no need for drugs if prompt and sufficient ventilation is provided

HARMFUL AND INEFFECTIVE RESUSCITATION PRACTICES

- Routine suction of new-born's mouth and nose as soon as the head is born
- Stimulation of the new-born by slapping or flicking the soles of the feet
- Postural drainage (putting the baby upside down) and slapping the back
- Squeezing the back to remove secretions from airway
- Routine giving of sodium bicarbonate to new-borns who are not breathing.
- Intubation by an unskilled person

FURTHER READING

1. Carlo WA, McClure EM, Chomba E, Chakraborty H, Hartwell T, Harris H, Lincetto O, Wright LL. Newborn care training of midwives and neonatal and perinatal mortality rates in a developing country. Pediatrics. 2010 Nov 1;126(5):e1064-71.
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16.13.9 SEIZURES, NEONATAL

BRIEF DESCRIPTION

- Seizures can be the most dramatic indication of neurologic abnormality in the newborn, yet most neonatal seizures are subtle or even silent.
- There are five types of neonatal seizures: Subtle seizures (presenting with apnea, starring, lip smacking, chewing or eye blinking); Focal clonic; Multifocal clonic; tonic, and Myoclonic seizures.
- The causes of neonatal seizures include metabolic, toxic, structural and infectious diseases.

CLINICAL FEATURES

- Neurologic signs like abnormal focal movements,
- Subtle manifestations like sucking movements

Investigations

- Laboratory –blood glucose level, electrolytes (calcium, magnesium),
- CSF analysis and CSF culture if meningitis is suspected,

TREATMENT

Objectives

- Terminate seizure
- Prevent brain damage
- Ensure appropriate brain development
- Prevent disability

Non-pharmacologic

Rule out metabolic disturbance that cause seizure like hypoglycemia, hypocalcemia

- Ensure patency of the airway
- Check breathing and circulation

Pharmacologic

INDICATION TO START AED

- Three or more seizure episodes in 24 hours 2 or more in one hour
- Any seizure associated with apnea or bradycardia

First line

- **Phenobarbital,** I.M/I.V/P.O.15-20 mg kg/day loading dose, followed by 5 mg/kg in two divided doses given after 24 hours after loading dose

Alternative

- **Phenytoin, I.M**/I.V/P.O.15-20 kg/day loading dose, followed by 5 mg/kg in two divided doses, given after 12 hour of the loading dose.

IF SEIZURES ARE ASSOCIATED WITH METABOLIC ABNORMALITIES,

- **Hypocalcemia (Hypocalcemic-tetany)**
  - **Calcium gluconate** solution, 10% 1-2 ml/kg/; repeat PRN after 6 hours

ADRs: bradycardia, cardiac arrest, extra vascular leakage may cause local necrosis.

  - **Hypoglycemia**
    - **Glucose** 10%, (For Dosage schedule, see under Hypoglycemia.)
  - **Vitamin B 6 deficiency**
    - **Vitamin B 6 (pyridoxine)**, 50mg IM as single dose

FURTHER READING

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16.13.10 SEPSIS IN THE NEWBORN

BRIEF DESCRIPTION

- Neonatal sepsis is defined as bacteremia with systemic manifestation in the absence of other primary systemic problems during the first 28 days of life.
- **Recognition of systemic sepsis** signs are usually non-specific since

other conditions cause similar clinical states (e.g., cardiac or respiratory failure, metabolic disorders)

- Neonatal sepsis can be divided into two subtypes: early vs late onset

EARLY ONSET SEPSIS:

- Occurs within the first 72 hours of life.
- It is caused by organisms prevalent in the genital tract of the mother or in the labour room, which includes mainly group B streptococci, *E coli*, Coagulase-negative Staphylococcus and L. monocytogenes.
- Majority of the neonates with early onset sepsis clinically manifest with respiratory distress due to intrauterine pneumonia.
- Early onset sepsis has usually fulminant course and high mortality.

LATE ONSET SEPSIS:

- The onset is delayed for a minimum of four days
- In most cases symptoms appear by the end of first week of life.
- About 2/3 cases of late onset septicemia are caused by gram negative bacilli while the rest are contributed by gram positive organisms.
- Meningitis is more frequent.

CLINICAL FEATURES

- Pallor, lethargy, jaundice, fever, hypothermia
- Temperature instability (note 1/3 of confirmed sepsis cases are normothermic)
- Hypoglycemia, increased respiratory rate, apnea, grunting, cyanosis
- Tachycardia, bradycardia episodes, poor perfusion, hypotension
- Petechiae, bleeding from puncture sites
- Poor feeding, vomiting, abdominal distension, feed intolerance
- Bilious aspirates/vomitus and loose stools

- Lethargy, irritability, seizures

INVESTIGATIONS

- Laboratory: - complete blood count, blood culture, CSF analysis and culture, urinalysis and culture, stool culture
- Chest X-ray

TREATMENT

- Any baby who is unwell must be considered at risk of sepsis and appropriate antibiotics commenced as soon as possible after taking cultures.
- Inability to obtain cultures should not delay administration of antibiotics.

OBJECTIVES

- Alleviate symptoms
- Avoid life-threatening complications
- Prevent multi-organ failure

Non-pharmacologic

- Maintenance of body temperature (Kangaroo mother care, radiant warmer, incubator)
- Adequate calorie and fluid maintenance
- Correction of associated metabolic abnormalities

PHARMACOLOGIC

- Till the culture report is collected start with broad-spectrum antibiotics, which includes penicillin and Aminoglycoside.

First line

- **Ampicillin**, 100 mg /kg/day every 12 hours IV.for 10 days.

PLUS

- **Gentamicin**, 5 mg/kg /day IV Daily for 10 days

Alternative

- **Penicillin G Sodium Crystalline**, 50,000IU/kg QID for ten days

PLUS

- **Gentamicin**, 5 mg/kg /day IV Daily for 10 days

FURTHER READING

1. Muhe LM, McClure EM, Nigussie AK, Mekasha A, Worku B, Worku A, Demtse A, Eshetu B, Tigabu Z, Gizaw MA, Workneh N. Major causes of death in preterm infants in selected hospitals in Ethiopia (SIP): a prospective, cross-sectional, observational study. The Lancet Global Health. 2019 Aug 1;7(8):e1130-8.
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16.13.11 MENINGITIS, NEONATAL

BRIEF DESCRIPTION

- Bacterial infection of the meninges in the first month of life.
- Meningitis may be associated with sepsis or present itself as a focal infection.
- Organisms causing neonatal meningitis are similar to those causing neonatal septicemia and pneumonia.

CAUSE

- The most common bacterial causes of neonatal meningitis are group B streptococcus, E. *coli and* Listeria.
- Meningitis due to group B streptococci:
    - These organisms often colonize the vagina and rectum of pregnant women, can be transmitted to babies during labor, and cause infection.

- Meningitis and septicemia during the 1st week after birth may be particularly severe.

CLINICAL FEATURES

- Initially, non-specific, including fever or hypothermia, failure to feed, vomiting, irritability, vomiting, feeding problems, apnoea
- Lethargy, seizure, full fontanel
- Nuchal rigidity, generally rare.

INVESTIGATIONS

- Lumbar puncture and Cerebrospinal fluid (CSF) analysis and culture, Blood culture
- White Blood Cell count and differential count

TREATMENT

Objectives

- Decrease the risk of grave complications and mortality
- Avoid residual sequelae
- Shorten hospital stay

Non-pharmacologic

- Restrict fluid intake to 70% of calculated maintenance
- Monitor urine output.
- Keep baby warm
- For high temperature control environment (undress), avoid paracetamol
- Prevent hypoglycaemia (breastfeeding if tolerated/possible, NGT or IV glucose)
- Ensure hydration/nutrition
- Give oxygen if needed (SpO_2 <92%)

Pharmacologic

First Line

- **Ampicillin**, 200mg/kg/day, IV every 12 hours for 14-21 days *PLUS* **Gentamicin**, 5mg/kg /day, IM every 24 hours for 14-21 days

Alternative

- If there is no response to the first line antibiotics within 48-72 of initiation of antibiotics, or if the infant has hospital acquired infection, or if the mother had culture proven gram-negative infection;
    - **Ampicillin** 200mg/kg/day, IV every 12 hours and **Cefotaxime** 50-75mg/kg every 8 hours.

      OR
    - **If the child is not jaundiced ➔Ceftriaxone**, 100mg/kg/24hr, IV in two divided doses (max. 4g/24hours *PLUS* **Ampicillin**, 200mg/kg/day, IV every 12 hours for 14-21 OR

FURTHER READING

1. Tewabe T, Mohammed S, Tilahun Y, Melaku B, Fenta M, Dagnaw T, Belachew A, Molla A, Belete H. Clinical outcome and risk factors of neonatal sepsis among neonates in Felege Hiwot referral Hospital, Bahir Dar, Amhara Regional State, North West Ethiopia 2016: a retrospective chart review. BMC research notes. 2017 Dec 1;10(1):265.
2. Kokeb M, Desta T. Institution Based prospective cross-sectional study on patterns of neonatal morbidity at Gondar University Hospital Neonatal Unit, North-West Ethiopia. Ethiopian journal of health sciences. 2016 Jan 21;26(1):73-9.

16.13.12 SYPHILIS, EARLY CONGENITAL

BRIEF DESCRIPTION

- It is a serious debilitating and disfiguring condition that can be fatal.
- About one third of syphilis-infected mothers have adverse pregnancy

outcome, one third give birth to a healthy baby, while the remaining third may result into congenital syphilis infection.

CAUSE

- Treponema pallidum bacteria

CLINICAL FEATURES

- May be asymptomatic
- Early congenital syphilis: begins to show after 6-8 weeks of delivery. Snuffle, palmar/plantar bullae, hepatosplenomegaly, pallor, joint swelling with or without paralysis and cutaneous lesions. These signs are non-specific.
- Late congenital syphilis: begins to show at 2 years. Microcephaly, depressed nasal bridge, arched palate, perforated nasal septum, failure to thrive, mental sub normality and musculoskeletal abnormalities

INVESTIGATIONS

- Preferably perform the tests on mother: VDRL/RPR.TPHA
- Assume cerebrospinal involvement in all babies less than 2 years

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

Non-pharmacologic

- Aqueous benzyl penicillin 150,000 IU/kg body weight IV every 12 hours for a total of 10 days OR procaine penicillin, 50,000 IU/kg body weight, IM single dose daily for 10 days
- Treat both parents for syphilis with benzathine penicillin 2.4 MU single dose (half on each buttock)

Note

- Assume that infants whose mothers had untreated syphilis or started treatment within 30 days of delivery have congenital syphilis
- If mother is diagnosed with syphilis during pregnancy, use benzathine penicillin as first line since erythromycin does not cross the placental barrier and therefore does not effectively prevent in utero acquisition of congenital syphilis
- Do not use doxycycline in pregnancy

PREVENTION

- Routine screening and treatment of syphilis infected mothers in antenatal clinics

FURTHER READING

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16.13.13 TETANUS, NEONATAL

BRIEF DESCRIPTION

- Neonatal tetanus is caused by infection of the umbilicus through cutting of the cord with unsterile instruments or from putting cow dung or other unsuitable materials on the stump

CLINICAL FEATURES

- Usually presents 3-14 days after birth with irritability and difficulty in feeding due to masseter (jaw muscle) spasm, rigidity, generalized muscle spasms.
- The neonate behaves normally for the first few days before the symptoms appear.

TREATMENT

Objectives

- Alleviate symptoms
- Avoid life-threatening complications

NON-PHARMACOLOGIC

- Refer to hospital immediately
- Nurse in quiet, dark and cool environment
- Suction the mouth and turn the infant 30 min after sedative. A mucous extractor or other suction should be available for use prn
- Ensure hydration/feeding
- Start with IV fluids (half saline and dextrose 5%)
- Put NGT and start feeding with expressed breast milk 24 hours after admission– in small frequent feeds
- Monitor and maintain body temperature
- Monitor cardiorespiratory function closely.
- Clean and debride the infected umbilicus

PHARMACOLOGIC

Neutralize toxin:

- Give tetanus immunoglobulin human (TIG) 500 IU IM. Give the dose in at least 2 different sites IM, different from the tetanus toxoid site. If this not available give TAT after skin test.
- Give 1st dose of PENTA vaccine

TREATMENT TO ELIMINATE SOURCE OF TOXIN

- First line antibiotics: Metronidazole loading dose 15 mg/kg over 60 min then, Infant <4 weeks: 7.5 mg/kg every 12 hours for 14 days, Infant >4 weeks: 7.5 mg/kg every 8 hours for 14 days

- Second line antibiotics: Benzyl penicillin 100,000 IU/kg every 12 hours for 10-14 days

CONTROL MUSCLE SPASM:

- Diazepam 0.2 mg/kg IV or 0.5 mg/kg rectal every 1 to 4 hours
- Other medicines: Chlorpromazine oral 1 mg/kg 8 hourly via NGT

PREVENTION

- Immunize all pregnant women during routine ANC visits
- Proper cord care

FURTHER READING

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CHAPTER 17:

SEXUALLY TRANSMITTED INFECTIONS (STI): SYNDROMIC MANAGEMENT OF STI

BRIEF DESCRIPTION

- STIs are serious and common problems worldwide. There are more than 20 types. Many of these are curable with effective treatment, but continue to be a major health problem for an individual and the community at large.
- With the emergence of HIV/AIDS the management of STIs makes more serious issue and calls for early screening, effective and urgent management.
- There are two basic approaches in the management of STIs namely etiologic diagnosis using laboratory tests and syndromic approach. The former approach is often regarded as the ideal way of diagnosing disease and the second one is the choice of resort when there are no laboratory facilities. Both classic approaches present with a number of problems.
- The syndromic case management has the following key features:
- It enables all trained first line health care providers to diagnose STI syndromes and treat patients on the spot, without waiting for laboratory results.
- It will help to offer treatment on the initial visit which is an important step to stop the spread of the disease.
- It is problem oriented (it responds to the patient's symptoms).
- It is highly sensitive and does not miss mixed infections.
- Uses flow charts that guide the health worker through logical steps.
- Provides opportunity and time for education and counseling.

NB: A number of different organisms that cause STIs give rise to only a limited number of syndromes.

- **A syndrome** is simply a group of symptoms a patient complains about and the clinical signs one can observe during examination of the patient.
- The aim of syndromic STI management is to identify one of the seven syndromes and manage accordingly. These are vaginal and urethral discharges, genital ulcer, lower abdominal pain, scrotal swelling, inguinal bubo and neonatal conjunctivitis.
- The syndromes are relatively easy to identify and it is possible to devise a flowchart, representing steps to be taken through a process of decision making, for each one.
- A major benefit of the flow chart is that, once trained, service providers find them easy to use- so non-STI specialists at any health facility are able to manage STI cases.

EACH FLOWCHART IS MADE UP OF A SERIES OF STEPS:

1. The clinical problem- the patient's presenting symptoms at the top; this is the starting point
2. A decision to make, usually by answering "yes" or "no" to a question
3. An action to take: what you need to do

17.1 URETHRAL DISCHARGE SYNDROME

- Urethral discharge is the presence of abnormal secretions from the distal part of the urethra and it is the characteristic manifestation of urethritis.
- Urethritis is usually due to sexually transmitted infections although urinary tract infections may produce similar symptoms.
- Urethral discharge is one of the commonest sexually transmitted infections among men in our country.

CAUSE OR ETIOLOGY OF UDS

- Urethral discharge can be caused by many different causative microorganisms (either single or polymicrobial).

- The two most common causative agents of the syndrome are Neisseria gonorrhea and Chlamydia trachomatis (81% and 36.8% respectively according the 2014 EPHI gonococcal antimicrobial sensitivity validation study).
- Some of the other causative micro-organisms are mycoplasma genitalium, Trichomonas vaginalis, and Ureaplasma urealyticum.

- Most of the time urethral discharge is due to mixed infection of Neisseria gonorrhea and Chlamydia trachomatis.
- In some rare cases it can be also the result of non-infectious causes.
- Due to these reasons urethral discharge is a syndrome of many causes rather than a single disease to be dealt with and it needs to be dealt with as a syndrome while it is being managed.

NB: Urethral discharge syndrome needs to be treated as soon as possible because if it is not treated on time it can cause serious complication.

CLINICAL MANIFESTATIONS OF UDS

- The common signs and symptoms of UDS are burning sensation (dysuria) during micturition, increased urgency and frequency of urination with itching sensation of the urethra.
- Urethral discharge: The amount and nature of the discharge vary according to the causative agents and other factors like prior treatments with antibiotics. The appearance of the discharge can be purulent or mucoid, clear, white, or yellowish-green.
- Sometimes it can be associated with scrotal swelling and pain which tends to be unilateral.
- The urethritis caused by N. gonorrhea has usually an acute onset with profuse and purulent discharge and the one caused by C. trachomatis has sub-acute onset with scant mucopurulent discharge.

COMPLICATIONS OF UDS

- Untreated UDS can cause some important acute and chronic complications. Hence early and prompt treatment of the syndrome is very important.

- Common acute complications
  - Disseminated gonococci syndrome
  - Perihepatitis
  - Acute epididymo-orchitis
- Common chronic complications
  - Urethral stricture
  - Infertility
  - Reiter's syndrome (the most common type of inflammatory polyarthritis in young men)

DIAGNOSIS OF UDS

- In properly managing the syndrome, the healthcare provider must take thorough and relevant history and do all relevant physical examinations.
- It must be noted that there is no need of lab investigations to identify the specific etiologic agents to manage the syndrome; it must be treated as a syndrome by sticking to syndromic case management which doesn't need to identify the specific cause.

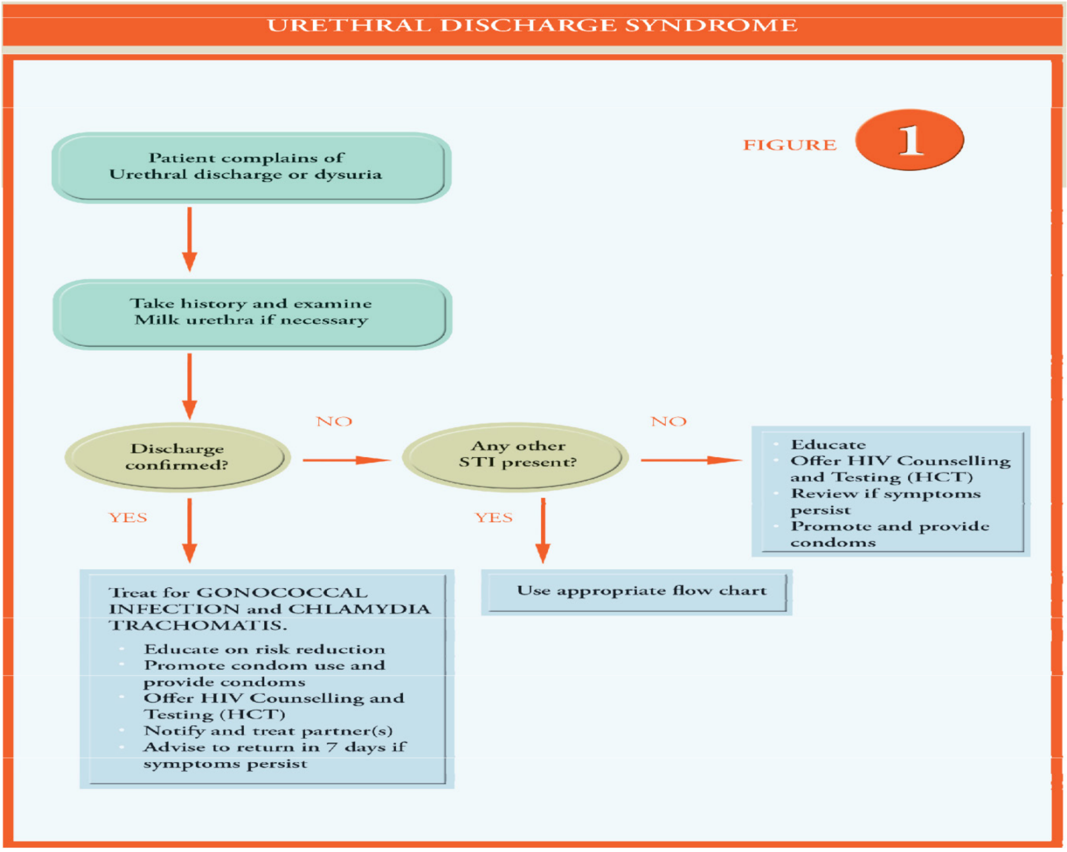

URETHRAL DISCHARGE SYNDROME
FIGURE 1
Patient complains of Urethral discharge or dysuria
Take history and examine Milk urethra if necessary
Discharge confirmed?
NO
Any other STI present?
NO
Educate
Offer HIV Counselling and Testing (HCT)
Review if symptoms persist
Promote and provide condoms
YES
Treat for GONOCOCCAL INFECTION and CHLAMYDIA TRACHOMATIS.
Educate on risk reduction
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
Notify and treat partner(s)
Advise to return in 7 days if symptoms persist
YES
Use appropriate flow chart

Figure 17.1:The algorithm of syndromic case management of urethral discharge syndrome (Adopted from the Ethiopian STI Guideline)

Treatment of UDS

Objectives

- Prevent long term complications including urethral stricture, infertility
- Prevent recurrence

Non pharmacologic

- None

Pharmacologic

- Treatment should target gonorrhea and chlamydial infections.

- In Ethiopia the recommended drugs of choice and their doses for the treatment of urethral discharge syndrome are:

First line (preferred)

- Ceftriaxone 250mg IM stat plus Azithromycin 1gm po stat

Alternative

- **Ciprofloxacin**, 500mg PO stat/**Spectinomycin** 2 gm IM stat PLUS **Doxycycline** 100 mg po bid for 7 days/**Tetracycline** 500 mg po QID for 7 days/**Erythromycin** 500 mg po QID for 7 days in cases of contraindications for Tetracycline (e.g. for children and pregnancy)

NB: Patients should be advised to return if symptoms persist for 7 days after the initiation of treatment. Single dose treatment is encouraged as much as possible

Note: In addition to treatment, the healthcare provider who is taking care of the patient with urethral discharge syndrome should educate the patient on

- Risk reduction
- Treatment compliance
- Proper and consistent use of condom
- Partner notification and management
- Importance of HIV testing
- Abstinence from sex till all symptoms resolve

17.2 PERSISTENT/RECURRENT URETHRAL DISCHARGE

- Some patients may complain of persistent or recurrent burning sensation or dysuria on urination, with or without discharge, due to various reasons.
  - Inadequate treatment or poor compliance and/or

  - Re-infection (partner/s not managed)
  - Persistent urethritis after Doxycycline based treatment might be caused by doxycycline-resistant M. genitalium
  - T. vaginalis is also known to cause Urethritis in men, hence the index patient should be treated for this.
  - Infection by drug-resistant organisms (N. gonorrhea)

Treatment of Persistent/Recurrent Urethritis Syndrome

Re-treat with initial regimen

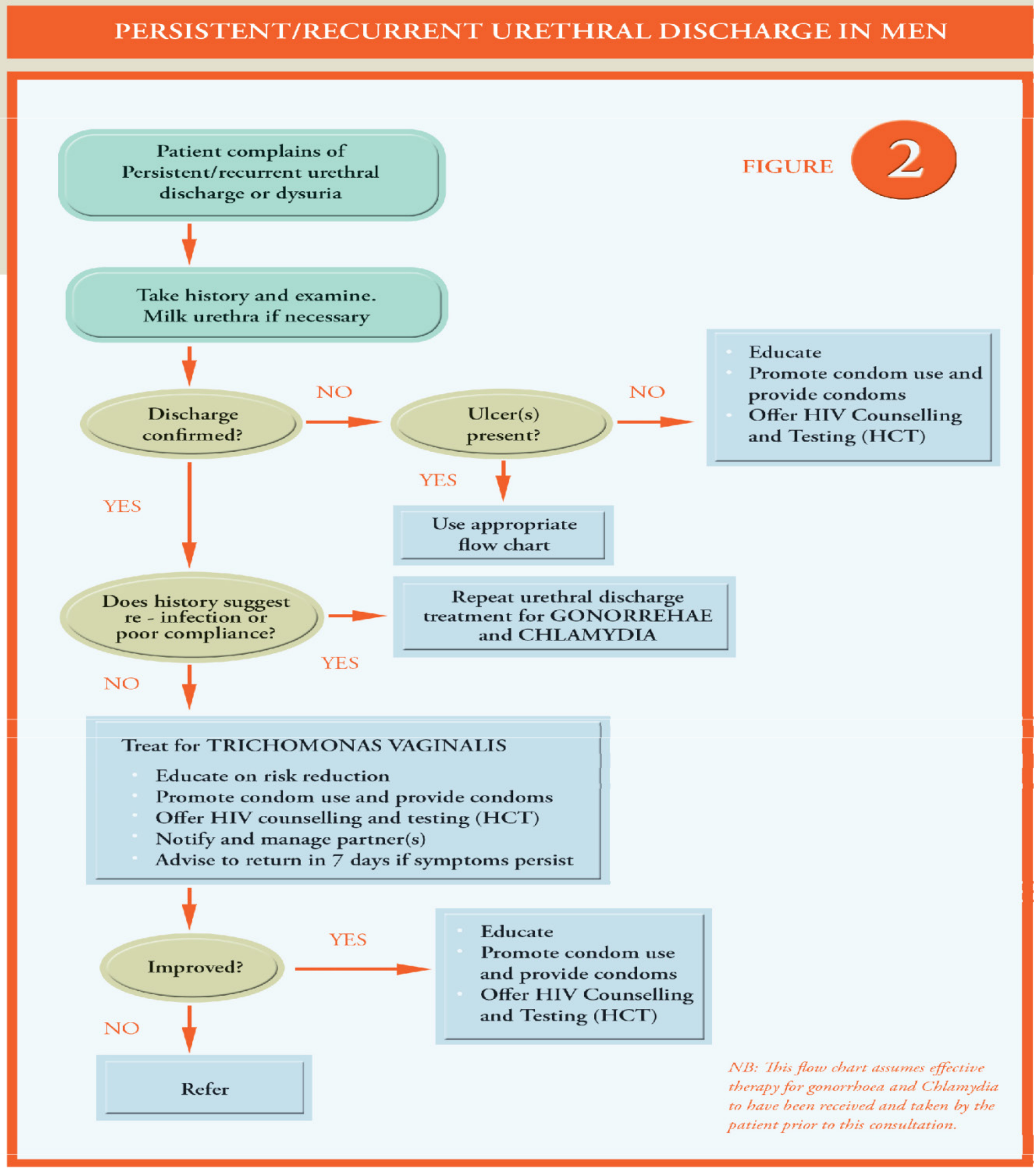
- If non-compliant or re-exposure occurs, re-treat with the initial regimen with due emphasis on drug compliance and/or partner management.
- Cover M. genitalium and T. vaginalis
- If compliant with initial regimen and re-exposure can be excluded, the recommended drug for persistent or recurrent urethral discharge syndrome in Ethiopia is:
  - Metronidazole 2 gm po. stat/Tinidazole 1gm po once for 3 days (Avoid Alcohol!)

    PLUS

  - Azithromycin 1 g orally in a single dose (only if not used during the initial episode to address doxycycline resistant M.genitalium)

REFERRAL

- Despite all these treatments, if symptoms still persist to require treatment with a new antibiotic regimen and a sexually transmitted agent is the suspected cause, all partners in the past 3 months before the initial diagnosis and any interim partners should be referred for evaluation and appropriate treatment of treatment failure.


PERSISTENT/RECURRENT URETHRAL DISCHARGE IN MEN
FIGURE 2
Patient complains of Persistent/recurrent urethral discharge or dysuria
Take history and examine. Milk urethra if necessary
Discharge confirmed?
NO
Ulcer(s) present?
NO
Educate
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
YES
Use appropriate flow chart
YES
Does history suggest re - infection or poor compliance?
YES
Repeat urethral discharge treatment for GONORREHAE and CHLAMYDIA
NO
Treat for TRICHOMONAS VAGINALIS
Educate on risk reduction
Promote condom use and provide condoms
Offer HIV counselling and testing (HCT)
Notify and manage partner(s)
Advise to return in 7 days if symptoms persist
Improved?
YES
Educate
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
NO
Refer

NB: This flow chart assumes effective therapy for gonorrhoea and Chlamydia to have been received and taken by the patient prior to this consultation.

Figure 17.2: The algorithm of syndromic case management of persistent or recurrent urethral discharge syndrome in men *(Adopted from the Ethiopian STI Guideline)*

17.3 GENITAL ULCER SYNDROME (GUS)

- Genital ulcer is an open sore or a break in the continuity of the skin or mucous membrane of the genitalia as a result of sexually acquired infections.
- Genital ulcer facilitates transmission of HIV more than other sexually transmitted infections because it disrupts continuity of skins and mucous membranes significantly.
- The relative prevalence of causative organisms for GUD varies from place to place; hence clinical differential diagnosis of genital ulcers is inaccurate in places where there are several etiologies.

ETIOLOGY OF GENITAL ULCER SYNDROME

- There are different kinds of bacteria and viruses which commonly cause genital ulcer.
- Some of the common etiologies of genital ulcer syndrome are:
  - Herpes simplex virus (HSV-1 and HSV-2)
  - Treponema pallidum
  - Haemophilius ducreyi (Chancroid)
  - Chlamydia trachomatis serovar L1, L2 & L3 (LGV)
  - Klebsiella granulomatis
- Most cases of genital herpes are caused by HSV-2. According to the validation study conducted in 2001, HSV2 alone was the leading cause of genital ulcer syndrome in both males and females constituting 44% and 76% of the cases respectively.
- Moreover, dual infection with other genital ulcer pathogens was found in 52% of males and 78% of females.

CLINICAL PRESENTATIONS

- Clinical manifestation and patterns of GUS may vary with presence of HIV infection.

- Genital ulcer has different kinds of clinical manifestations due to different causatives.
- Common clinical manifestations of genital ulcer are:
    - o Constitutional symptoms such as fever, headache, malaise and muscular pain
    - o Recurrent painful vesicles and irritations
    - o Shallow and non-indurated tender ulcers
    - o Common sites in male are glance penis, prepuce and penile shaft
    - o Common sites in women are vulva, perineum, vagina and cervix and can cause occasionally severe vulvo- vaginitis and necrotizing cervicitis
    - o Painless indurated ulcer (Chancre)
    - o Regional lymph adenopathy
- Syphilis: Clinically has three stages (primary, secondary, tertiary). The ulcer starts during the primary stage of the disease as papules & rapidly ulcerate. The ulcer is typically painless, clean base and raised boarder.
- Genital herpes: herpes simplex virus is the most common causes of genital ulcer worldwide. It produces lifelong infection after the primary infection (latency). The lesions are painful, erythematous macules which progressively form vesicles, pustules, ulcer and crusts.
- Chancroid: is also the common cause of genital ulcer in developing countries. The lesion started as painful papules and pustules which ulcerate with dirty base and soft edge. Inguinal fluctuant adenopathy (buboes) may occur following ulcer.
- Lymphogranuloma veneurum (LGV): The disease starts as painless papules that develops an ulcer. After a few days painful regional lymphadenopathy develop and associated systemic symptoms may occur.
- Granuloma inguinale (Donovanosis): is chronically progressive ulcerative disease without systemic symptoms, presents with non-suppurative painless genital ulcer and beefy-red appearance

Complications of genital ulcer syndrome

- Locally destructive granulomatous lesions occur (Gummas) on the skin, liver, bones, or other organs
- Tabes dorsalis and dementia, often with paranoid features
- Latent meningovascular parenchymatous
- Optic atrophy
- General paresis
- Aortic aneurysm and aortic valve insufficiency
- Asymptomatic aortitis
- Angina pectoris
- Recurrent disease
- Aseptic meningitis
- Encephalitis
- Phimosis in men
- Destruction of the penis or auto amputation
- Extra genital lesions

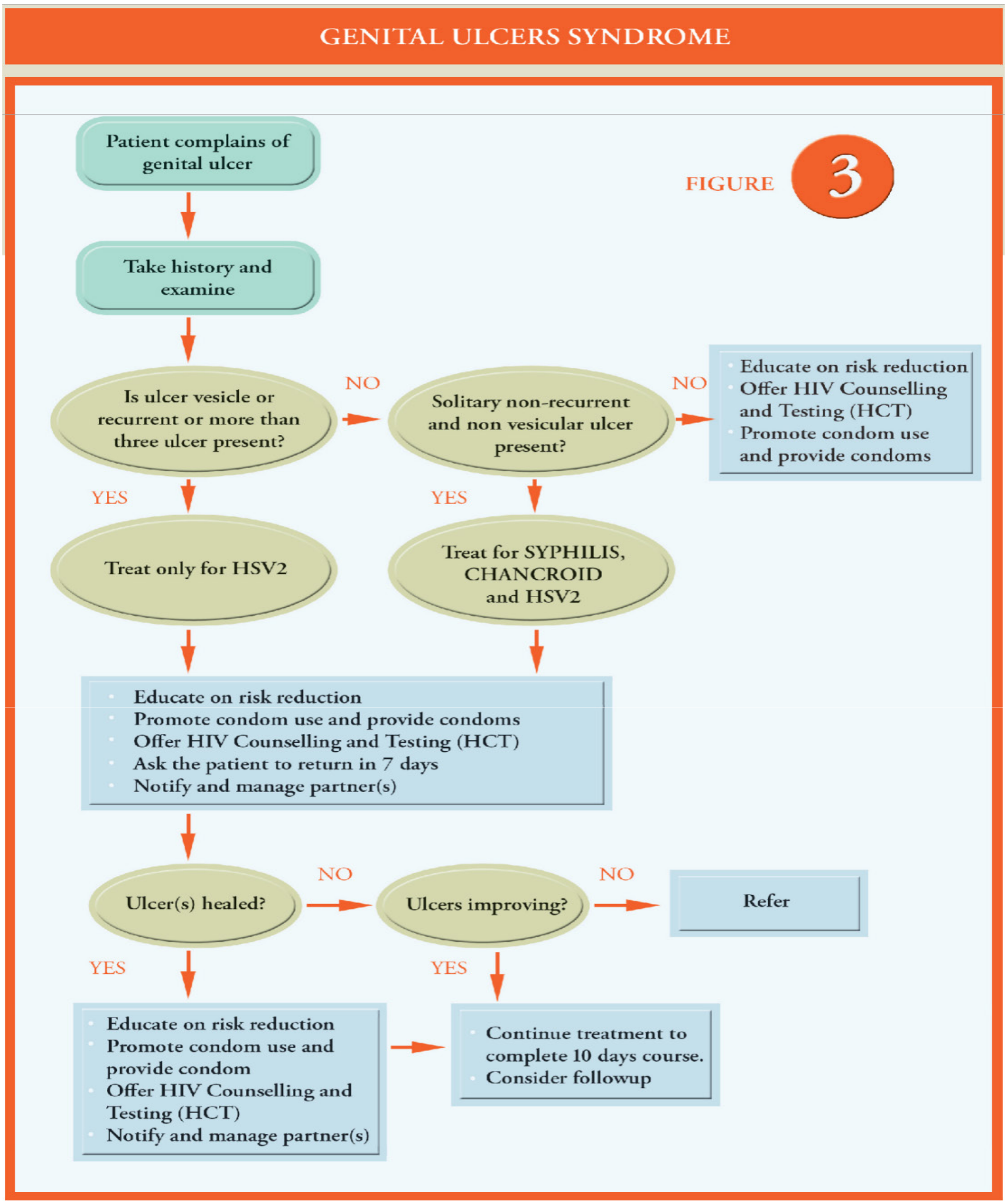

GENITAL ULCERS SYNDROME
FIGURE 3
Patient complains of genital ulcer
Take history and examine
Is ulcer vesicle or recurrent or more than three ulcer present?
NO
Solitary non-recurrent and non vesicular ulcer present?
NO
Educate on risk reduction
Offer HIV Counselling and Testing (HCT)
Promote condom use and provide condoms
YES
Treat only for HSV2
YES
Treat for SYPHILIS, CHANCROID and HSV2
Educate on risk reduction
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
Ask the patient to return in 7 days
Notify and manage partner(s)
Ulcer(s) healed?
NO
Ulcers improving?
NO
Refer
YES
Educate on risk reduction
Promote condom use and provide condom
Offer HIV Counselling and Testing (HCT)
Notify and manage partner(s)
YES
Continue treatment to complete 10 days course.
Consider followup

Figure 17.3: The algorithm of syndromic case management of genital ulcer syndrome (Adopted from the Ethiopian STI Guideline)

Treatment of genital ulcer syndrome

- To avoid the complications, some of which are life threatening as mentioned above, the syndrome must be treated aggressively and promptly.
- Objective
- Screen patient for HIV and other ulcerative STIs
- Prevent long term complications
- Halt the transmission of the infection

Non-pharmacologic

- Prevent secondary infection by local cleaning

Pharmacologic

- The recommended treatment regimen for genital ulcer in Ethiopia is depicted below.

1. TREATMENT FOR NON- VESICULAR GENITAL ULCER

- Benzathine penicillin 2.4 million units IM stat/Doxycycline (in penicillin allergy) 100mg bid for 14 days,

  PLUS

- Ciprofloxacin 500mg bid orally for 3 days /Erythromycin 500mg tab QID for 7 days

  PLUS

- Acyclovir 400mg TID orally for 10 days (or 200 mg five times per day of 10 day)

2. TREATMENT FOR VESICULAR, MULTIPLE OR RECURRENT GENITAL ULCER

- Acyclovir 200 mg five times per day for 10 days Or Acyclovir 400 mg TID for 7 days
- N.B. There is no medically proven role for topical acyclovir, its use is discouraged.

3. TREATMENT FOR RECURRENT INFECTION EPISODES:

- Treatment should be initiated during prodrome or immediately after onset of symptoms.
- Local care: Keep affected area clean and dry
- Acyclovir 400 mg P.O. TID for 5 to 7 days,

Suppressive treatment: recommended for patients with 6 recurrences or more per year

- Acyclovir, 400mg P.O. BID for 1 year

N.B. The need for continued suppressive therapy should be reassessed.

17.4 VAGINAL DISCHARGE

BRIEF DESCRIPTION

- Abnormal vaginal discharge in terms of quantity, color or odor could be most commonly as a result of vaginal infections.
- But it is a poor indicator of cervicitis, especially in young girls because a large proportion of them are asymptomatic.
- The most common causes of vaginal discharge are Neisseria gonorrhoeae, Chlamydia trachomati, Trichomonas vaginalis, Gardnerella vaginalis (Polymicrobial), Candida albicans.
- The first three are sexually acquired and the last two are endogenous infections etiologic agents.
- Bacterial vaginosis (Gardnerella vaginalis) is the leading cause of vaginal discharge in Ethiopia followed by candidiasis, trichomoniasis, gonococcal and chlamydia cervicitis in that order.

RISK ASSESSMENT

- Major risk factor for cervicitis using vaginal discharge as an entry point to manage cervical infection is far from ideal.

- While vaginal discharge is highly indicative of vaginal infection, it is poorly predictive of cervical infection with gonorrhea and/or chlamydia.
- The flowchart may become more predictive of cervical infection if a number of risk factors indicative of cervical infection are included.

N.B. One or more of the following are risk factors for STI related cervicitis in Ethiopia

- Multiple sexual partners in the last 3months.
- New sexual partner in the last 3 months
- Ever traded sex
- Age below 25 years

NB: The presences of one or more risk factor suggest cervicitis.

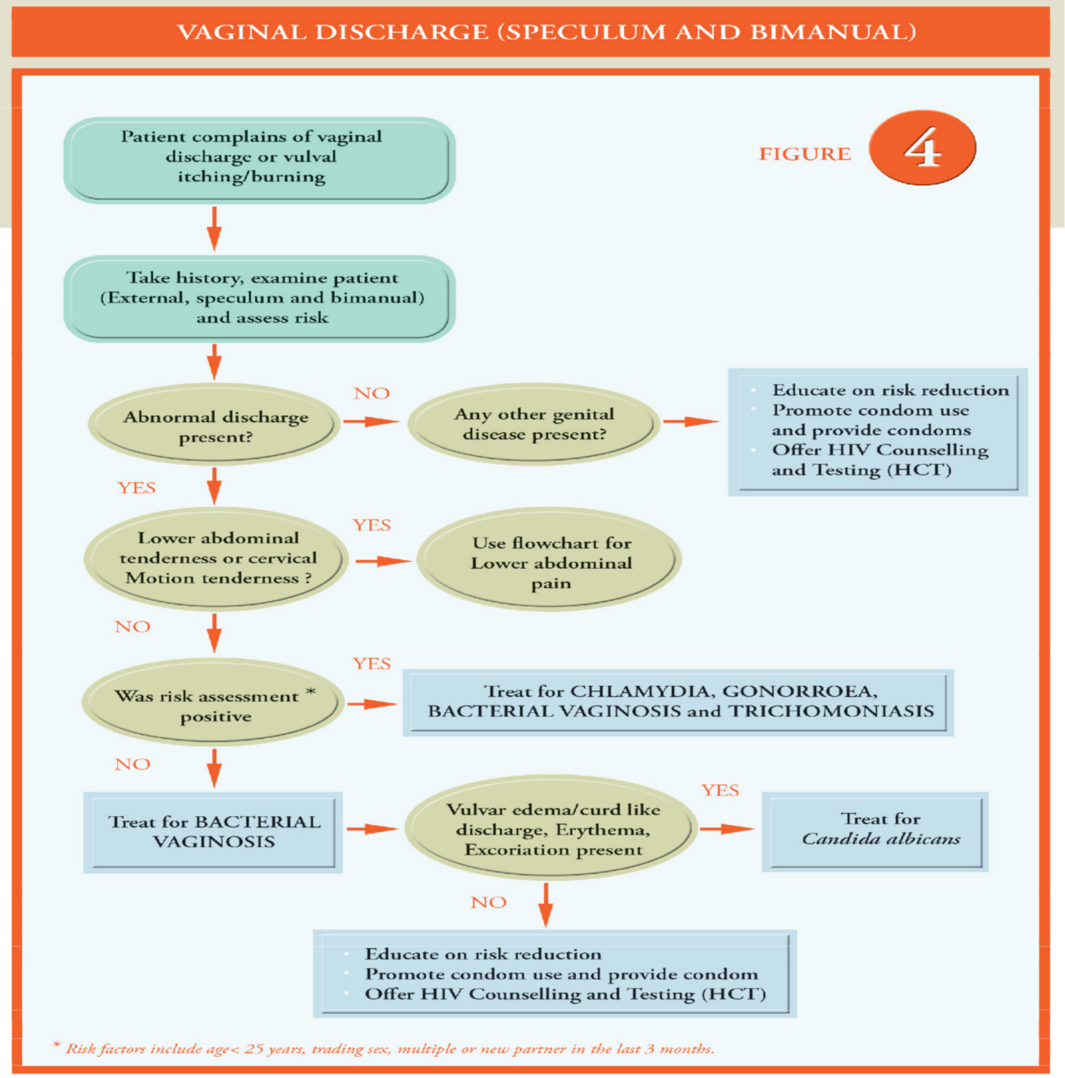

VAGINAL DISCHARGE (SPECULUM AND BIMANUAL)
FIGURE 4
Patient complains of vaginal discharge or vulval itching/burning
Take history, examine patient (External, speculum and bimanual) and assess risk
Abnormal discharge present?
NO
Any other genital disease present?
Educate on risk reduction
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
YES
Lower abdominal tenderness or cervical Motion tenderness ?
YES
Use flowchart for Lower abdominal pain
NO
Was risk assessment * positive
YES
Treat for CHLAMYDIA, GONORROEA, BACTERIAL VAGINOSIS and TRICHOMONIASIS
NO
Treat for BACTERIAL VAGINOSIS
Vulvar edema/curd like discharge, Erythema, Excoriation present
YES
Treat for Candida albicans
NO
Educate on risk reduction
Promote condom use and provide condom
Offer HIV Counselling and Testing (HCT)
* Risk factors include age< 25 years, trading sex, multiple or new partner in the last 3 months.

Figure 17.4. The algorithm of syndromic case management of vaginal discharge (Adopted from the Ethiopian STI Guideline)

TREATMENT

- Vaginal discharge syndrome can cause devastating complications if left untreated.
- Hence any woman with vaginal discharge syndrome must be treated promptly.

PHARMACOLOGIC

- If **Risk assessment positive:**
  - Ceftriaxone 250mg IM stat/Ciprofloxacin 500mg po stat/ Spectinomycin 2 gm IM stat PLUS Azithromycin 1gm po stat/Doxycycline 100 mg po bid for 7 days PLUS Metronidazole 500 mg bid for 7 days
  - If discharge is white or curd-like add Clotrimazole vaginal pessary 200 mg at bed time for 3 days
  - Note: The preferred regimen is Ceftriaxone 250mg IM stat + Azithromycin 1gm po stat + Metronidazole 500 mg bid for 7days
- **If risk assessment negative**
  - **Metronidazole** 500 mg bid for 7 days
  - If discharge is white or curd-like add
  - **Clotrimazole** vaginal pessary 200 mg at bed time for 3 days, OR miconazole vaginal pessary 200mg at bed time for 3 days.

SEX PARTNERS

- Examination and treatment usually not necessary if the risk assessment is negative.
- However, treatment with an imidazole cream (e.g., miconazole, clotrimazole) may be indicated in some cases of recurrent infection, or if the partner has penile candidiasis (Balanitis).

17.5 LOWER ABDOMINAL PAIN

BRIEF DESCRIPTION

- All sexually active women presenting with lower abdominal pain should be carefully evaluated for the presence of upper genital tract infections (tube, uterus, ovaries, and pelvic cavity).
- In addition, all women with presumptive STI should undergo thorough

bimanual and abdominal examination because some of the women with PID may not complain of lower abdominal pain.

- Other suggestive symptoms include pain during intercourse, vaginal discharge, abnormal vaginal bleeding (inter-menstrual), painful urination, pain during menstruation, fever and sometimes nausea and vomiting.
- PID is difficult to diagnose because the clinical manifestations widely vary. PID becomes highly probable when one or more of the above symptoms are seen in a woman with adnexal tenderness, vaginal discharge and cervical motion tenderness.

INDICATIONS FOR PATIENT'S REFERRAL WITH ACUTE PID

- The diagnosis is uncertain
- Surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded
- A pelvic mass is suspected
- Severe illness precludes management on an outpatient basis
- The patient is pregnant
- The patient is unable to follow or tolerate an outpatient regimen; or
- The patient has failed to respond to outpatient treatment.

N.B. Many experts recommend that all patients with PID should be admitted to hospital for treatment.

- The most common causative agents responsible for this syndrome include N. gonorrhea, C. trachomatis, and anaerobic bacteria.
- Facultative Gram-negative rods and Mycoplasma hominis are also implicated sometimes.
- As it is difficult to differentiate between these clinically, and a precise microbiological diagnosis is nearly impossible in most clinical set ups, hence the treatment regimen must be effective against the incriminated microorganisms.

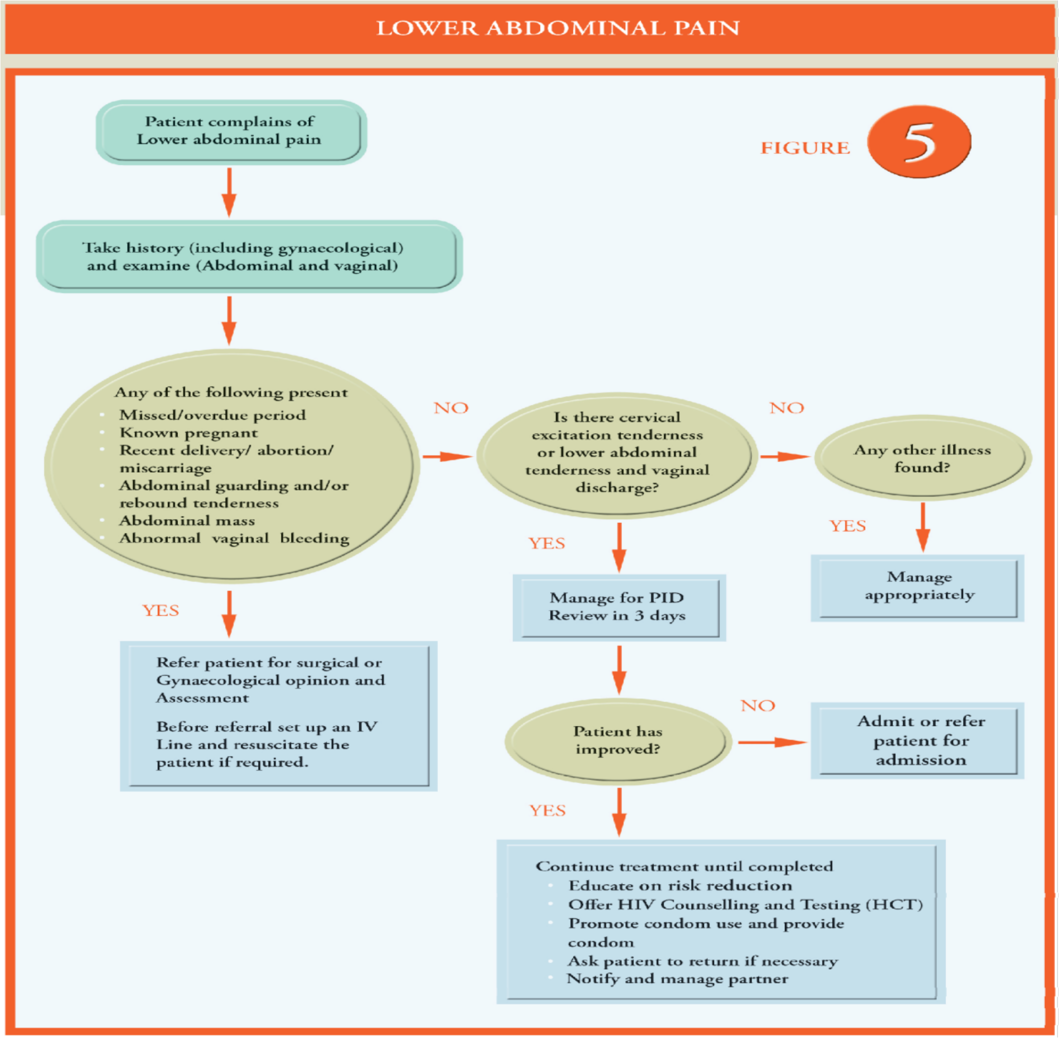

LOWER ABDOMINAL PAIN
FIGURE 5
Patient complains of Lower abdominal pain
Take history (including gynaecological) and examine (Abdominal and vaginal)
Any of the following present
Missed/overdue period
Known pregnant
Recent delivery/ abortion/ miscarriage
Abdominal guarding and/or rebound tenderness
Abdominal mass
Abnormal vaginal bleeding
NO
Is there cervical excitation tenderness or lower abdominal tenderness and vaginal discharge?
NO
Any other illness found?
YES
Manage appropriately
YES
Manage for PID Review in 3 days
YES
Refer patient for surgical or Gynaecological opinion and Assessment
Before referral set up an IV Line and resuscitate the patient if required.
Patient has improved?
NO
Admit or refer patient for admission
YES
Continue treatment until completed
Educate on risk reduction
Offer HIV Counselling and Testing (HCT)
Promote condom use and provide condom
Ask patient to return if necessary
Notify and manage partner

Figure 17.5:The algorithm of syndromic case management of lower abdominal pain (Adopted from the Ethiopian STI Guideline)

Treatment

Pharmacologic

For outpatients

- **Ceftriaxone** 250 mg IM stat/ Ciprofloxacin, 500mg po single dose/ **Spectinomycin** 2gm i.m stat PLUS **Azithromycin** 1gm po stat/ **Doxycycline** 100 mg po b.i.d for 14 days PLUS **Metronidazole** 500 mg po b.i.d for 14 days

- Admit if there is no improvement within 72 hours

Note: The preferred regimen is **Ceftriaxone** 250mg IM stat PLUS **Azithromycin** 1gm po stat PLUS **Metronidazole** 500 mg bid for 14 days

FOR HOSPITALIZED PATIENTS (INPATIENTS)

- **Ceftriaxone** 250 mg i.m/i.v /**Spectinomycin** 2 gm i.m bid PLUS **Azithromycin** 1gm po daily /**Doxycycline** 100 mg po b.i.d for 14 days PLUS **Metronidazole** 500 mg po b.i.d for 14 days

Note: For inpatient PID, **ceftriaxone**, **spectinomycin** or **azithromycin** should continue for 24hrs after the patient remain clinically improved, after which **doxycycline** and **metronidazole** should continue for a total of 14 days

17.6 SCROTAL SWELLING

Brief description

- Inflammation of the epididymis usually manifests with acute onset of unilateral testicular swelling, often with tenderness of the epididymis and vas deferens, and occasionally with erythema and edema of the overlying skin.
- When it occurs in young male (<35 years old) accompanied with urethral discharge it is usually due to gonococcal or chlamydial infections.
- In older people the etiologic agent may be non-STIs such as E. coli, Klebsiella spp. or Pseudomonas.
- TB orchitis is generally accompanied by an epididymitis

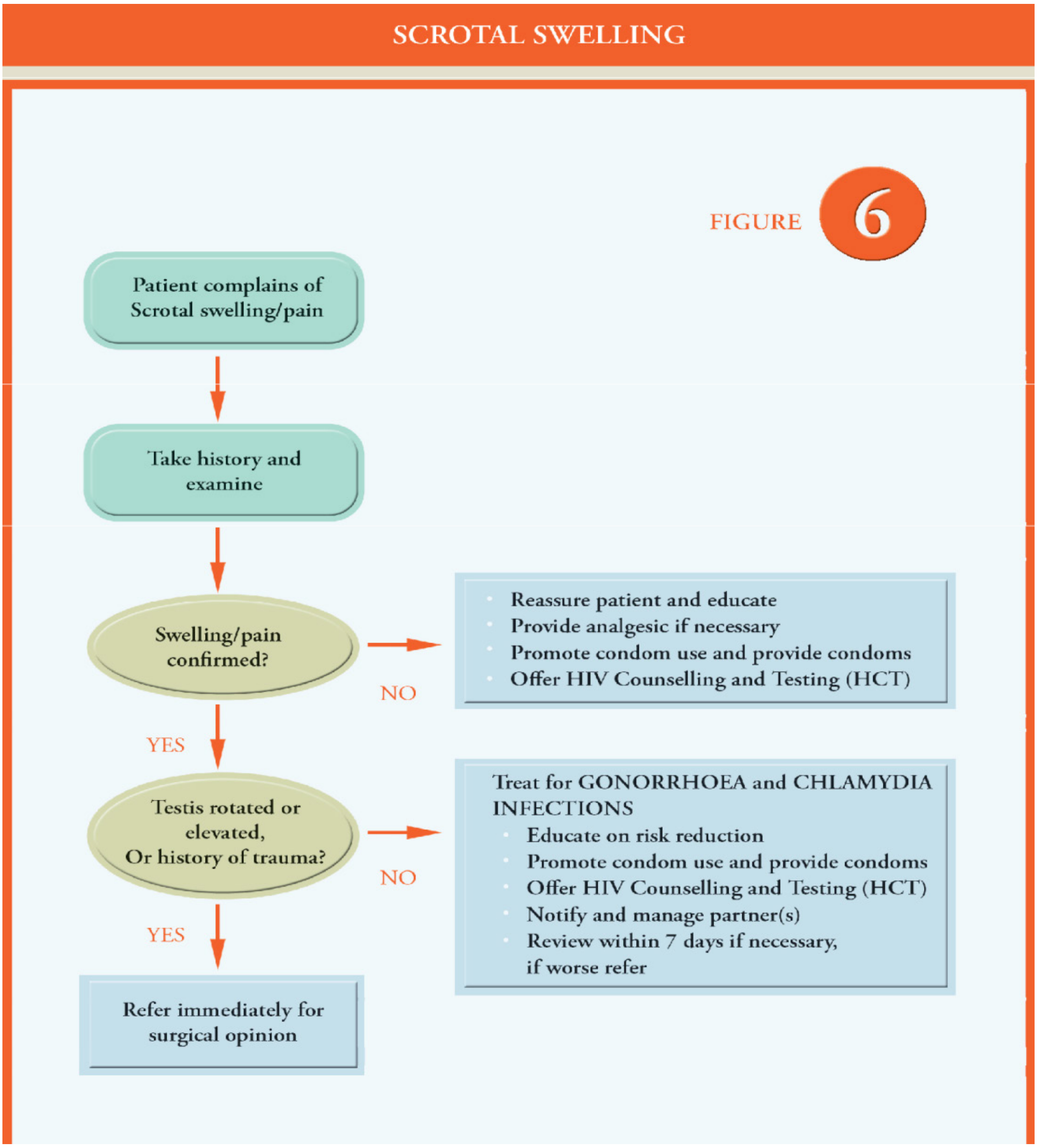

SCROTAL SWELLING
FIGURE 6
Patient complains of Scrotal swelling/pain
Take history and examine
Swelling/pain confirmed?
NO
Reassure patient and educate
Provide analgesic if necessary
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
YES
Testis rotated or elevated, Or history of trauma?
NO
Treat for GONORRHOEA and CHLAMYDIA INFECTIONS
Educate on risk reduction
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
Notify and manage partner(s)
Review within 7 days if necessary, if worse refer
YES
Refer immediately for surgical opinion

Figure 17.6: The algorithm of syndromic case management of Scrotal Swelling (Adopted from the Ethiopian STI Guideline)

TREATMENT

- If quick and effective therapy is not given, the complications (Destruction and scarring of testicular tissues, infertility, impotence, and prostatitis) may occur.

- The treatment of scrotal swelling suspected of STI origin is similar to that of urethral discharge and thus the following drugs are recommended.
- In addition, analgesia and scrotal support may be indicated as required.

Non-pharmacologic:

- Scrotal support

PHARMACOLOGIC

First line (preferred)

- Ceftriaxone 250mg IM stat plus Azithromycin 1gm po stat

Alternative

- Ciprofloxacin, 500mg PO stat/Spectinomycin 2 gm IM stat PLUS Doxycycline 100 mg po bid for 7 days/Tetracycline 500 mg po QID for 7 days/Erythromycin 500 mg po QID for 7 days in cases of contraindications for Tetracycline (e.g. for children and pregnancy)

17.7 INGUINAL BUBO

BRIEF DESCRIPTION

- This is a painful, fluctuant, swelling of the lymph nodes in the inguinal region (groin). Buboes are usually caused by either chancroid or LGV.
- In many cases of chancroid, but not all, an associated ulcer is visible.
- Infection of the lower limb and other non-STIs like TB can also cause swelling of the inguinal lymph nodes.

ETIOLOGY

- The common causes of inguinal and femoral bubo are:
  - Chlamydia trachomatis (L1, L2 and L3) (causes LGV)
  - Klebsiella granulomatis (donovanosis)
  - Treponema pallidum (causes syphilis)
  - Haemophilius ducreyia (causes chancroid)

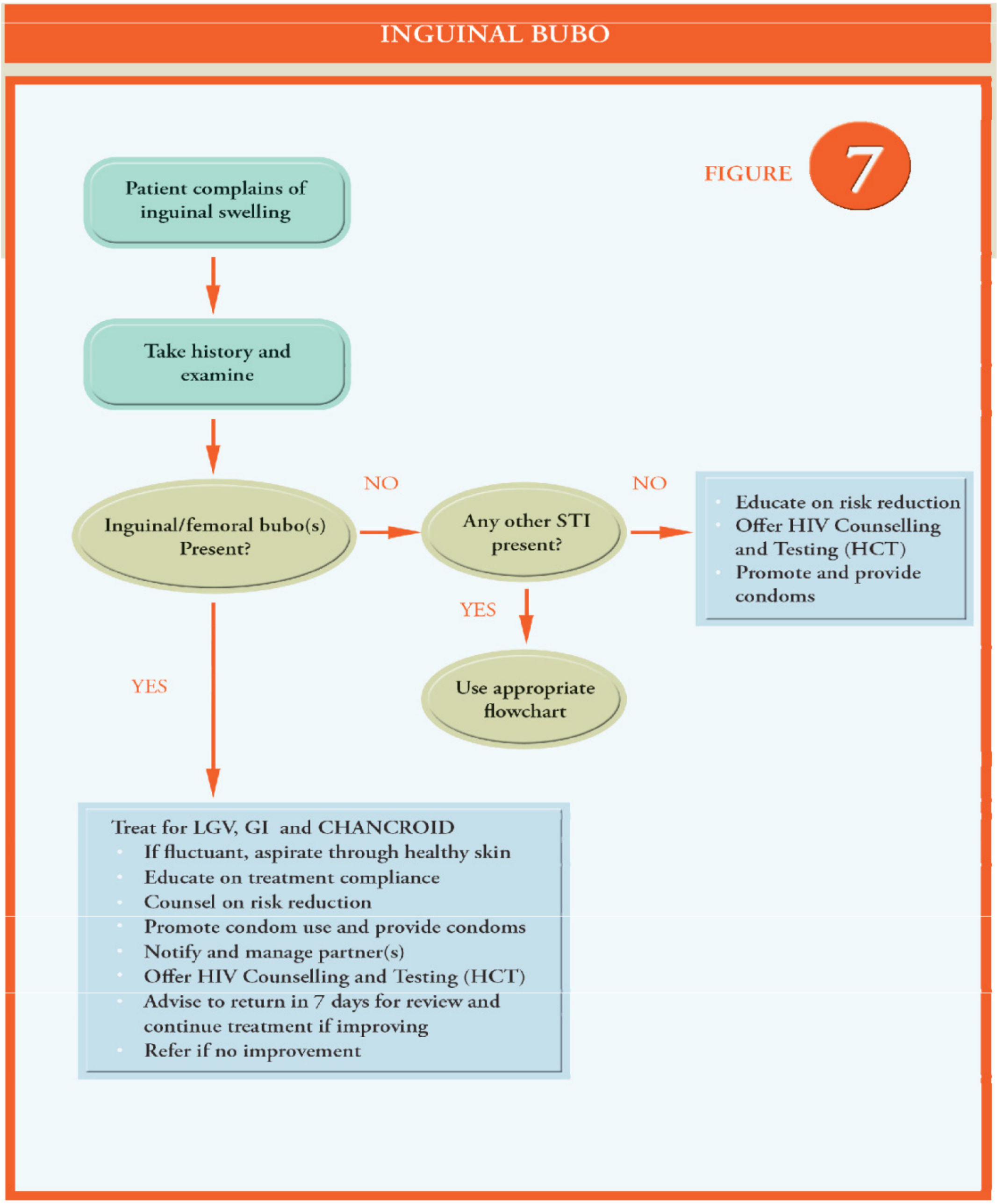

INGUINAL BUBO
FIGURE 7
Patient complains of inguinal swelling
Take history and examine
Inguinal/femoral bubo(s) Present?
NO
Any other STI present?
NO
Educate on risk reduction
Offer HIV Counselling and Testing (HCT)
Promote and provide condoms
YES
Use appropriate flowchart
YES
Treat for LGV, GI and CHANCROID
If fluctuant, aspirate through healthy skin
Educate on treatment compliance
Counsel on risk reduction
Promote condom use and provide condoms
Notify and manage partner(s)
Offer HIV Counselling and Testing (HCT)
Advise to return in 7 days for review and continue treatment if improving
Refer if no improvement

Figure 17.7:The algorithm of syndromic case management of urethral discharge syndrome (Adopted from the Ethiopian STI Guideline)

TREATMENT

Objectives

- Prevent complication, which includes fistula formation, lymphatic obstruction
- Screen for other STIs

Non pharmacologic:

- Keep the lesion clean and dry

Pharmacologic

First line

- **Ciprofloxacin**, 500mg P.O, BID for 3days

PLUS

- **Doxycycline**, 100mg P.O, BID for 14days OR **Erythromycin**, 500mg, P.O, QID for 14days
- If patient have genital ulcer, add **Acyclovir** 400mg tid orally for 10 days (or 200mg five times per day for 10 days)

N.B. Fluctuant lymph nodes should be aspirated through healthy skin but incision and drainage or excision of nodes may delay healing and should not be attempted.

REFERRAL

- Referral is indicated where there is doubt with diagnosis and/or treatment failure.

NB: The term 'refer' stand for;

- at General hospital where culture and sensitivity test is available, do the test and treat accordingly.
- But if culture and sensitivity test is not available, the term 'refer' indicates to refer the patient to regional or central lab where culture and sensitivity test and DNA PCR (polymerase chain reaction) are available and then treat the patient according

17.8 BALANITIS/ BALANOPOSTHITIS (BAL)

BRIEF DESCRIPTION

- Balanitis is inflammation of the glans penis, and balanoposthitis includes inflammation of the foreskin.

COMPLICATIONS:

- Phimosis is a constriction of opening of foreskin in a way not retracted over the glans penis.
- Paraphimosis is trapping of foreskin behind glans penis. It requires urgent reduction by urologist.

CAUSE:

- The most common causes:
- Inadequate personal hygiene in uncircumcised males.
- candidal infection

OTHER CAUSES

- Various infectious agents, dermatologic conditions, and premalignant conditions.

CLINICAL FEATURES

- Present with pain, tenderness, or pruritus associated with erythematous lesions on the glans and/or the foreskin; an exudate may also be present.

INVESTIGATION AND DIAGNOSIS

- Inspect the glans and foreskin and urethral meatus for inflammation/ discharge.
- Inspect for possible paraphimosis (trapping of the foreskin behind glans penis).
- History and physical examination findings may indicate specific etiologies for management consideration

- History of diabetes mellitus or HIV infection or white, curd-like exudate may suggest candidal infection.
- Purulent or foul-smelling exudate may suggest bacterial infection
- Behavioral risk(s) for sexually transmitted infections may imply Trichomonas, herpes simplex virus (HSV), human papillomavirus, scabies, or Mycoplasma genitalium.
- Vesicular or ulcerative lesions may imply HSV or syphilis
- History of generalized dermatitis (Psoriasis, eczema, lichen planus), Erythematous scaly plaques (Psoriasis)
- Pruritic purplish plaques (Lichen planus)
- Constitutional symptoms; polyarthritis (Circinate balanitis)
- Small, painless, ulcerative lesions with a serpiginous border (Circinate balanitis)

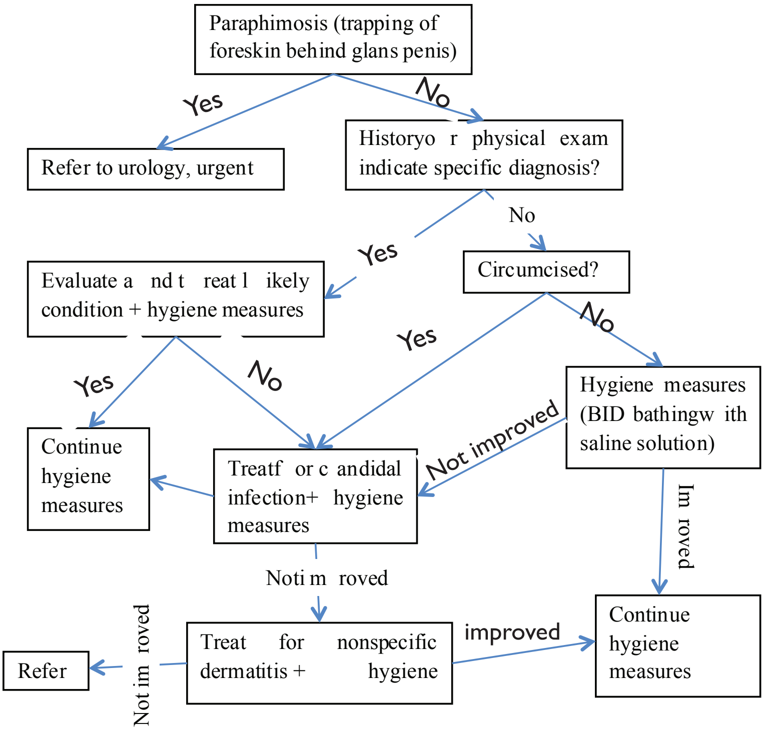

Paraphimosis (trapping of foreskin behind glans penis)
Yes
No
Refer to urology, urgent
Historyo r physical exam indicate specific diagnosis?
No
Yes
Circumcised?
Evaluate a nd t reat l ikely condition + hygiene measures
Yes
No
Yes
No
Hygiene measures (BID bathingw ith saline solution)
Continue hygiene measures
Treatf or c andidal infection+ hygiene measures
Not improved
Im roved
Noti m roved
Not im roved
Refer
Treat for nonspecific dermatitis + hygiene
improved
Continue hygiene measures

Figure 17.8: Diagnostic evaluation and management of balanitis (Adopted from the Ethiopian STI Guideline)

TREATMENT

HISTORY OR PHYSICAL EXAM SUGGEST SPECIFIC DIAGNOSIS

- Evaluate and treat based on the likely condition or etiology (generally treat with topical antibiotics for bacterial infections, topical steroid creams for dermatologic conditions, and potential ablation or excision for premalignant lesions).

No identified cause (History or physical exam do not suggest specific diagnosis)

- Hygiene measures (retraction of the foreskin and thorough genital cleansing (twice daily bathing of affected area) with saline solution, alone for uncircumcised males), PLUS
- Empiric treatment for candidal infection (for uncircumcised males and/or noninfectious dermatitis is warranted in some patients (usually if no response with antifungal therapy).

IF NOT RESPOND TO SALINE SOLUTION BATHING
(CIRCUMCISED AND UNCIRCUMCISED males):

- Empiric treatment for candidal infection with clotrimazole 1% twice daily or miconazole 2% twice daily for 7 days.

IF NO IMPROVEMENT ON ANTIFUNGAL THERAPY
(CIRCUMCISED AND UNCIRCUMCISED MALES):

- A trial of hydrocortisone 1% cream twice daily for 7 days for nonspecific dermatitis. If allergic to imidazoles use Nystatin cream 100,000 units/g; for severe symptoms: a single dose of oral fluconazole 150 mg or the combination a topical imidazole and hydrocortisone 1% cream.

IF NO IMPROVEMENT ON EMPIRIC
NONSPECIFIC DERMATITIS THERAPY

- Refer to dermatology or urology for consideration of biopsy to evaluate for other dermatologic causes and/or to rule out pre-malignant lesions.

17.9 SYPHILIS SCREENING AND MANAGEMENT

BRIEF DESCRIPTION

- Syphilis is caused by the bacterium Treponema pallidum.
- During initial stage of infection, the organism spreads widely, setting the point for consecutive manifestations.
- Syphilis is important health concern for women, especially HIV-infected women.
- In Ethiopia, the estimated syphilis prevalence among ANC attendees in 2012 was 1%, indicating a low prevalence of syphilis in pregnant women (RPR >5% indicates high prevalence).
- Adverse pregnancy outcomes such as miscarriage or stillbirth, congenital syphilis in the new born and progression of latent syphilis in the mother are anticipated complications if the mother is left untreated.
- Thus, RPR test should be routinely done on pregnant mothers in their first trimester and treatment should be instituted if the rapid plasma regain (RPR) test is reactive.

STAGING AND CLINICAL MANIFESTATIONS

- Each stage of syphilis has characteristic clinical presentations not altered by pregnancy

EARLY SYPHILIS

- **Primary syphilis:** Typically involves of a solitary painless chancre at site of inoculation, complemented by local adenopathy.
- **Secondary syphilis:** A systemic illness often including a rash (disseminated or involving palms and soles), malaise, fever, and other symptoms such as pharyngitis, mucous patches, hepatitis, condyloma lata, alopecia.
- **Early latent:** Period infection with *T. pallidum* as demonstrated by serologic testing, but no symptoms. Occurs within first year of initial infection.

LATE SYPHILIS

- **Tertiary syphilis:** Late syphilis with symptomatic manifestations involving the cardiovascular system or gummatous disease (granulomatous disease of skin and subcutaneous tissues, viscera, or bones).
- **Late latent syphilis:** Period of infection with *T. pallidum* as demonstrated by serologic testing, but no symptoms. Occurs after one year after initial infection, but if timing of infection is not known, late latent syphilis is presumed.

NEUROSYPHILIS

- May happen at any time in the course of infection.
- **Early neurosyphilis:** may have asymptomatic meningitis; symptomatic meningitis; or less commonly meningovascular disease (ie, meningitis and stroke).Vision or hearing loss with or without concomitant meningitis may also be present, and ocular/otologic syphilis is treated as neurosyphilis.
- **Late neurosyphilis:** The most common forms involve brain and spinal cord (dementia - general paresis and tabes dorsalis).

COMPLICATIONS OF SYPHILIS

- If untreated, have a number of significant late manifestations or complications, including cardiovascular, gummatous, and neurologic.

INVESTIGATIONS

- Diagnostic testing should be made for all patients with signs and symptoms of syphilis.
- Asymptomatic patients had better be screened for syphilis if at high risk for acquired disease or for transmitting infection to others (eg, pregnancy).

DIAGNOSIS

- Diagnostic evaluation for syphilis is the same in pregnant and nonpregnant women.
- A diagnosis of syphilis is made using serologic testing of blood specimens (presumptive, diagnosis than definitive).

- A diagnosis is made when both nontreponemal and treponemal tests are reactive.
- Nevertheless, either test can be used as the initial screening test. But due to high possibility of false positive screening test results, confirmatory testing is necessary.
- If neurosyphilis considered, additional cerebrospinal fluid analysis should be performed.
- **Appropriate interpretation of serologic testing** (depends on clinical disease presence or absence, patient's prior syphilis history, and individual's immune status). examples:
    - ○ **If no prior syphilis history:** diagnosis made if both nontreponemal & treponemal tests are reactive.
    - ○ **If has history of treated syphilis:** a positive nontreponemal test may suggest a new infection, evolving response to recent therapy, treatment failure, or presence of a serofast state.
- A positive nontreponemal test followed by a negative treponemal test: generally considered a false positive result.
- An initial treponemal-specific screening may have a positive treponemal test followed by a negative nontreponemal test. This is usually seen for previously treated syphilis. Also, in very early syphilis (occasional), or in late syphilis when nontreponemal tests become nonreactive over time.
- Patient with clinical signs and symptoms of early syphilis (eg, ulcer, rash) may have false negative result for initial nontreponemal test, classically due to testing prior to antibody formation or secondary to a prozone effect.
- **Latent syphilis:** diagnosed if no clinical signs or symptoms of syphilis but has serologic evidence of infection. Early or late latent depending upon duration of infection- if duration unknown considers it as late syphilis.
- All diagnosed cases of new syphilis should be treated, tested for HIV and other sexually transmitted diseases.

SCREENING

- Pregnant women should be screened for syphilis:
    - All pregnant women: screen at the first prenatal encounter
    - Women at high risk of infection: repeat screening at 28 to 32 weeks and at delivery
    - Women who have not been screened in pregnancy or who deliver a stillborn after 20 weeks of gestation: screen at delivery
- False-positive screening tests may be more common in the setting of pregnancy. Thus, confirmatory testing must be performed (algorithm)

PRE-TREATMENT EVALUATION

- A nontreponemal titer should be obtained just before starting therapy (preferably, on the first day of therapy) since titers can increase significantly over a few days between diagnosis of syphilis and treatment initiation.

TREATMENT

- Penicillin remains the gold standard treatment for syphilis in both pregnant and nonpregnant patients appropriate for their stage of infection.
    - Parenteral (IM or IV) penicillin G is the only therapy with recognized efficacy and safety for both mother and fetus during pregnancy.
    - Alternatives are not as safe for pregnant woman or fetus or not as effective for prevention of congenital syphilis.
    - It is effective for treating maternal disease, preventing transmission to the fetus, and treating established fetal disease.
    - Hence, penicillin desensitization is recommended for infected pregnant women with known penicillin allergy.
- If penicillin desensitization is not possible, World Health Organization (WHO) recommends the following:
    - For early syphilis (primary, secondary, or latent <2 years), suggests using, with caution, erythromycin 500 mg orally four times daily for 14 days or ceftriaxone 1 g intramuscularly once daily for 10–14 days or azithromycin 2 g once orally (high resistance to azithromycin is likely, avoid).

- For treatment of late syphilis ((more than two years' duration) or unknown stage of syphilis), with erythromycin 500 mg orally 4 QID for 30 days.
- Since macrolides do not completely cross placental barrier; hence, WHO also recommends infants born to mothers treated with non-penicillin agents receive a 10-to-15-day course of parenteral penicillin treatment.

Table 17.1: Treatment of syphilis for pregnant and non-pregnant adults with normal renal function (Adopted from the Ethiopian STI Guideline)

Stage of syphilis*	**Treatment**	
	Non-pregnant adults	**Pregnant adults**
Early syphilis (Primary/ secondary/ early latent)	**First line:** • Penicillin G benzathine 2.4 million units IM once **Alternatives (choose one):** • Doxycycline 100 mg orally BID for 14 days • Ceftriaxone 1 to 2 g daily IM or IV for 10 to 14 days • Tetracycline 500 mg orally QID for 14 days • Amoxicillin 3 g plus probenecid 500 mg, both given orally BID for 14 days	Penicillin G benzathine (Bicillin L-A) 2.4 million units (MU) IM in a single dose (administer as 1.2 MU in each buttock) **If serologic failure on follow-up:** additional follow-up not assured, Prompt CSF and retreating as late syphilis is recommended.

Late syphilis (Late latent/ tertiary/ unknown duration)	First line: • Penicillin G benzathine 2.4 million units IM once weekly for three weeks Alternatives (choose one): • Doxycycline 100 mg orally BID for four weeks • Ceftriaxone 2 g daily IM or IV for 10 to 14 days	Penicillin G benzathine (Bicillin L-A) 2.4 million units IM once weekly (administer as 1.2 MU in each buttock) for 3 weeks (7.2 million units total dose) **If a dose is missed for > 14 days**, restart the full 3 dose course of therapy.
Neurosyphilis (including ocular syphilis); *After IV treatment completion, single dose of 2.4 MU PGB (for non-pregnant) and once/week for 3 weeks (pregnant) can be used*	Preferred: • Aqueous penicillin G 3 to 4 million units IV every four hours (or 18 to 24 million units continuous IV infusion) for 10 to 14 days§ • Penicillin G procaine 2.4 million units IM daily plus probenecid 500 mg orally QID, both for 10 to 14 days • If possible, desensitize allergic patients and treated with IV penicillin **Alternatives:** • Ceftriaxone 2 g IV daily for 10 to 14 days • doxycycline (200 mg orally BID) for 21 to 28 days (If no ceftriaxone or allergic to it)	Aqueous crystalline penicillin G (intravenous) 18 to 24 MU per day, administered as 3 to 4 MU IV every 4 hours or as a continuous infusion over 24 hours for 10 to 14 days OR Penicillin G procaine 2.4 million units IM once daily (usually administered as 1.2 MU in each buttock) plus probenecid 500 mg PO 4 times daily, both for 10 to 14 days
Post-exposure prophylaxis	See discussion below	Penicillin G benzathine (Bicillin L-A) 2.4 million units IM in a single dose (administer as 1.2 MU in each buttock)

*The National STI Guideline (2015) consider and manage a history of non-reactive RPR test within the past 2 years as early syphilis and infections more than two years ago or no prior history of non-reactive RPR test (unknown duration) as late syphilis.

COMPLICATIONS OF TREATMENT AMONG PREGNANTS

- Jarisch-Herxheimer reaction: this may precipitate uterine contractions, preterm labor, and/or non-reassuring fetal heart rate tracing in pregnant women treated in the second half of pregnancy.
- Provide supportive care of maternal distress and standard obstetric management of pregnancy complications.

FOLLOW-UP (USING CLINICAL ASSESSMENT AND SEROLOGY TEST)

i) Monitor clinically and with serologic testing after treatment to ensure response.

ii) **Frequency of nontreponemal titers;**

- The same test, preferably RPR, should be done each time and at the same laboratory.
- A fourfold increase in nontreponemal titer after treatment is always abnormal.
- A fourfold decrease in titer, equivalent to a change of two dilutions (such as from 1:16 to 1:4 or 1:32 to 1:8), is considered as acceptable response to therapy; but this may take months to attain.
- For pregnants a fall in maternal titers does not guarantee that fetal treatment has been adequate.
- Over time, most successfully treated syphilis patients experience seroreversion; but some may remain serofast.

iii) Frequency of serologic monitoring depends on stage of disease & existence of HIV:

- In HIV-uninfected with early syphilis: test at 6- and 12-months following treatment and at any time if clinical symptoms recur. In general, such patients experience adequate response by 12 months.

- HIV-uninfected with late syphilis: follow-up serologic testing at 6, 12, and 24 months. Some with late syphilis may not have adequate response for up to 2 years after treatment.
- HIV co-infected: should be monitored more frequently.

  v) Neurosyphilis: Monitored at same frequency as without neurosyphilis. Additional, monitoring of cerebrospinal fluid abnormalities is necessary.

  vi) **Pregnant women**

- Women on early syphilis: check a titer just before treatment, as it is common for this titer to be higher than initial diagnostic titer due to lapsed time between diagnosis and treatment.
- Subsequent follow-up frequency is the same to nonpregnants and depends on stage of disease and HIV coinfection.

HANDLING TREATMENT FAILURE

- Suspect failure if nontreponemal titers do not decline fourfold or greater, or if fourfold increase after an initial decline.
- If no adequate response to treatment, determine if reinfected, experiencing a slow response to treatment, or has failed treatment.
- Treatment failure is likely due to poor adherence, alternative agent use, immunosuppressed status, or unrecognized CNS disease.

TREATMENT AFTER AN EXPOSURE

- Sexually partners:
  - ○ Should be evaluated clinically and serologically for evidence of infection.
  - ○ Empiric treatment requirement depends primarily upon when the exposure occurred and the stage of their partner's infection.

VERTICAL TRANSMISSION (VT)

- Frequency is higher with early than late-stage syphilis.
- Among women who acquire syphilis during pregnancy, the risk of VT increases with increasing gestational age at acquisition of maternal infection.

- Fetal infection should be suspected if there are characteristic findings on ultrasound examination after 20 weeks of gestation in a woman with untreated or inadequately treated syphilis.
- Hepatomegaly and placentomegaly are early findings suggestive of congenital syphilis.
- Anemia, ascites and hydrops occur later in course of fetal infection.
- An abnormal ultrasound is not diagnostic and the normal also does not exclude fetal infection.

FETAL TREATMENT

- Maternal penicillin treatment is curative for fetal infection in most cases.
- A maternal treatment ≤30 day before delivery is a risk factor for congenital infection.
- A maternal treatment with non-penicillin agents is also a risk factor.
- Aqueous crystalline penicillin G 50, 000 units/kg IV tid for 10-15 days OR procaine penicillin G 50,000 units/kg IM daily for 10 -15 days for prevention (at risk cases) and treatment of congenital syphilis.

17.10 GENITAL WARTS

BRIEF DESCRIPTION

- Genital warts affect both men and women and can occur at any age.
- Most patients with genital warts are between the ages of 17-33 years.
- Genital warts are highly contagious.
- There is around a 60% risk of getting the infection from a single sexual contact with someone who has genital warts.
- In children younger than three years of age, genital warts are thought to be transmitted by nonsexual methods such as direct manual contact.

- Nevertheless, presence of genital warts in children should raise suspicion for sexual abuse.
- The peak time for acquiring infection for both women and men is shortly after becoming sexually active.
- HPV is sexually transmitted, but penetrative sex is not required for transmission.
- Skin-to-skin genital contact is a well-recognized mode of transmission.

ETIOLOGY

- Genital warts are caused by the human papilloma virus (HPV). About 90% of genital warts are caused by two specific types of the Human Papilloma virus with a low cancer-causing potential. The viruses are:
- Human papilloma virus (HPV-6)
- Human papilloma virus (HPV-11)
- HPV type 16, 18, 31 and 45 (high risk of oncogenicity)

CLINICAL MANIFESTATIONS

- In men, genital warts can infect the urethra, penis, and scrotum.
- The warts can appear as soft, raised masses with a surface that can be smooth or rough with many fingerlike projections.
- Others may appear pearly, cauliflower- like, or rough with a slightly dark surface.
- Most lesions are raised, but some may be flat or papillary with only

COMPLICATIONS

- Common complications of genital warts are:
- Extensive anogenital warts

- Laryngeal papilloma in the infant (passage of HPV from the mother to infant at birth)
- Squamous cell carcinoma
- Carcinoma of the cervix

TREATMENT OF EXTERNAL GENITAL WARTS

- The primary goal of treatment of genital wart is to eliminate the symptoms caused by the visible warts. Eradication of the virus and elimination of infectivity is difficult to achieve.
- The recommended treatment regimen for genital warts in Ethiopia is:

PATIENT APPLIED:

First line

- **Imiquimod** 5% cream to be applied directly on the warts 3 times per week for up to 16 weeks if available.
- The treatment area should be washed with soap and water 6-10 hours after application.

Alternative

- Topical application of Podophylotoxin 0.5% bid for 3 days followed by 4 days of no treatment the cycle continued up to 4 times if available.
- Hands should be washed immediately after application.

Provider administered:

- **Trichloroacetic** acid (TCA) (30-90%) weekly base, applied carefully to the warts avoiding normal tissue.
- **TCA** should be applied to genital wart after applying vasline to surrounding normal skin.
- **Podophylin** resin 10-25% to be applied on the warts, avoiding normal

tissue.

- Wash thoroughly 1-4 hours after application.
- Treatment should be repeated at weekly intervals until wart resolve.
- Cryotherapy
- Surgical removal
- Surgical removal should be spared for giant warts (surgical intervention for small warts might cause dissemination)

Note:

- Referral of patients with meatal or cervical warts is necessary for cryotherapy or surgical removal.
- Do not use podophylin toxin and resin during pregnancy.

17.11 GENITAL SCABIES

BRIEF DESCRIPTION

- Scabies is a condition of very itchy skin caused by tiny mites Sarcoptes scabiei that burrow into the skin.
- Sarcoptes scabiei is transmitted by close skin to skin contact with an infested case.
    - This includes sexual, non- sexual or social transmission within families, at schools and with workmates.
- The sites commonly affected are the pubis, penis, lower abdomen, scrotum, vulva and perianal region. The mites may, however spread to other hairy parts of the body such as chest, armpits, eyelashes and eye brows, but not to the scalp.

CLINICAL MANIFESTATIONS

- Itching is the main complaint.
- Erythematous papules and burrows tunneled by female mite can be seen using a hand lens.
- Some patients may be completely unaware and lice are spotted on routine clinical examination; therefore, careful examination under a good light is necessary.

TREATMENT

Non-pharmacologic

- Washing clothes in hot water or ironing clothes after normal washing.

Pharmacologic

First line

- Permethrin 5%, thin films of cream applied to all areas of body from the neck down for 8-14 hrs. then washed off.
- Reapplication after one week is advised.
- It is recommended especially for infants above the age of 2 months, children and adults.

Alternative

- Benzyl Benzoate 25%, applied to entire body, neck to toe for 3 to 5 consecutive evenings.
- Give 12.5% for children
- Bath should be taken before the first and after the last application.
- Sulphur ointment: Children 5%, Adult 10%:
- thinly applied to the entire body for 3 consecutive nights.
- The patient should wash thoroughly before each new application and 24 hours after the last treatment.
- It is not recommended for infants less than 2 months age and pregnant women.

17.12 PEDICULOSIS PUBIS

BRIEF DESCRIPTION

- The pubic louse (Phthirus pubis) is transmitted by sexual contact and can produce itching around the pubic area.
- The parasite can spread to the thighs, chest, and axillae and even to the eye lids.
- The diagnosis is established by clinical examination, as the parasite is visible by naked eyes.

TREATMENT

Objectives

- Completely delouse the patient to prevent recurrence and transmission to fellow individuals.

Non pharmacologic

- Launder all clothes, sheets, blankets in hot water
- Iron all clothing
- Shave the pubic area

Pharmacologic

First line

- Permethrin, thin films of 1% or 5 % cream, applied for 10 minutes then washed
- Should be applied below the neck
- Vaseline can be applied if it involves the eye brows and eyelash (suffocation method).

Alternatives

- Benzyl benzoate, 25% emulsion applied once.

17.13 PREVENTION OF STIS

- Comprehensive approach to STI prevention includes risk assessment with counseling, vaccination, identification of infected individuals and effective treatment with follow-up, and evaluation and treatment of sexual partners.
- Accurate risk assessment, education and counseling of at-risk individuals to avoid STIs
- Carefully obtain routine sexual histories for proper screening and prevention counseling.
- Behavioral risk factors include:
- New or multiple sex partners,
- sex partners with recent STI,
- no or inconsistent condom use outside a monogamous sexual partnership,
- Commercial sex work for money or drugs,
- Sex workers or sexual contact with them.
- Careful evaluation of adolescents and pregnant is important for the high risk for STI.
- All individuals evaluated for STI screening or diagnosis should be tested for HIV infection.
- Patient-centered risk reduction counseling:
- assess patient's understanding of STI transmission risk,
- discuss risk of patient's sexual behavior,
- assessing patient's willingness to change behavior,
- have shared goal for behavioral change, with clear & realistic steps.
- Prevention may include abstinence, mutual monogamy, barrier methods (Male and female condoms).
- Use of male condoms has been associated with a reduced risk for HIV, chlamydia, gonorrhea, HSV, and HPV transmission.

VACCINATION:

- Pre-exposure vaccinations of at-risk individuals for vaccine-preventable infections avoid several sexually transmitted or associated infections:
- Hepatitis A virus (HAV) vaccine, individuals with chronic liver disease, and those with risk factors for HAV infection (like illicit drug use).
- Hepatitis B virus (HBV) vaccine, for nonimmune individuals with STI risk factors, comprising injection drug users and HIV-infected ones.
- Human papillomavirus (HPV) vaccine, Gardasil have recently been developed to prevent HPV type 16 and 18 infections which are associated with 80% of cervical cancer. It is offered to all girls who are age 14 in Ethiopia.
- Meningococcal vaccine, for persons exposed to outbreaks, HIV-infected ones, among others.
    - Identification of both asymptomatic and symptomatic individuals with STIs can avoid unrecognized transmission.
    - Effective diagnosis, treatment, counseling, and follow-up of infected individuals is alos critical component of STI prevention.
    - Sex partners of infected individuals should also be evaluated, treated, and counseled to prevent persistent infection transmission.
- **Other prevention methods:**
    - Male circumcision: may reduce HIV acquisition; also decrease risk of HSV and HPV infection.
    - Antimicrobial-based prevention may include: antiretroviral treatment (pre-exposure prophylaxis, and post-exposure prophylaxis, to prevent HIV infection). Suppressive antiviral therapy for genital herpes simplex virus (HSV) can prevent transmission.

FURTHER READING

1. Ministry of Health (MOH). MOH National Guidelines for the Management of Sexually Transmitted Infections Using Syndromic Approach. Addis Ababa: July 2015
2. World Health Organization (WHO). WHO guideline on syphilis screening and treatment for pregnant women. Geneva: WHO; 2017. Available at https://www.who.int/reproductivehealth/publications/rtis/syphilis-ANC-screenandtreat-guidelines/en/

CHAPTER 18:

SKIN DISEASES

BRIEF DESCRIPTION

- Dermatologic diseases represent one of the most common causes of morbidity in developing countries such as Ethiopia.
- Few reports indicate the true burden of cutaneous diseases in Ethiopia, according to some studies; up to 80% of the populations have one or more skin diseases in their life time.
- Skin disease is one of the most common cause of morbidity in Ethiopia and it represent the sixth most frequent cause of outpatient visits to health care facilities nationwide.
- The prevalence of Dermatologic diseases in developing countries are very high particularly infections and infestations account the majority of cases which is attributed to environmental factors, poor hygiene, overcrowding and lack of access to dermatologic care.
- Nowadays in addition to communicable skin diseases other skin conditions such as eczema, inflammatory skin disorders, pigmentary disorders, connective tissue disorders and skin tumors are increasing in number.
- Treatment modalities for skin diseases can be broadly categorized into medical therapy (topical and systemic) and physical therapy (e.g., cryotherapy, phototherapy, laser and surgery).
- Topical therapy is suitable for localized and less severe skin conditions. Examples are topical steroids, topical retinoids.
- Systemic therapy is used for extensive and more serious skin conditions or if topical treatment is ineffective or if there is systemic involvement.

18.1 GENERAL GUIDELINE FOR USE OF TOPICAL STEROIDS

- The topical corticosteroids are the back bone of topical dermatological therapy and are among the most commonly prescribed medication in an outpatient dermatology setting.
- Variety of topical steroids is available and this available range of formulations and potency gives flexibility to treat all groups of patients, different phases of disease, and different anatomic sites.
- Topical steroids are classified into mild, moderate, potent and very potent according to their strength.
- Usually, 30gm per tube is enough to cover the whole body.
- It has anti-inflammatory and anti-proliferative effect.
- Topical steroids are usually used for allergic and immunologic reaction, inflammatory skin conditions, bullous and blistering disorders and connective tissue disease.
- Unfortunately, topical steroids are misused in many countries and have led to significant unwanted effects.
- The rapid use in incidence of improper use of these drugs by general physicians, dermatologists and patients threatens to bring a much bigger problem.
- Even the most potent corticosteroids can be found in beauty and cosmetics shops mixed with other products.
- These drugs should be banned from ordinary shops all of them should be strictly prescription drugs.
- Benefits of rational and ethical use and the harm of overuse and misuse for nonmedical, especially cosmetic purposes should be clearly conveyed before prescribing steroids.
- For effective and wise treatment with topical steroids, key factors to be considered are:

  - Accurate diagnosis
  - Selecting the correct drug, keeping in mind the potency and delivery vehicle
  - Knowing the dose, frequency of application, duration and adverse effects and
  - Proper patient profiling
- Topical steroids have different side effects including skin atrophy, blanching, acne, striae, hypertrichosis, hyper pigmentation and increased infection risks.
- Rarely systemic side effects can occur and include immunosuppression, osteoporosis, hypertension, diabetes mellitus and psychiatric abnormality.
- To minimize side effects and optimize the use of topical steroid, the following principles should be followed:
  - Topical steroids should only be prescribed after appropriate diagnosis
  - Use appropriate potency and strength of steroids to achieve disease control
  - Any concomitant infections should be treated before using steroids
  - Discontinuation should be gradual after prolonged application
  - Be extra careful when prescribing steroid over certain areas (face, scrotum and flexures)
  - Be especially considerate when prescribing to the elderly and children

18.2 DRY SKIN

BRIEF DESCRIPTION

- Dry skin also called xerosis is a common problem.
- Dry skin can have several causes including aging, malnutrition, atopic eczema, renal insufficiency, dry climate and excessive exposure to water and soap.

CLINICAL FEATURES

- Xerotic skin appears dry, dull with fine scales. If dryness is severe: itching, erythema, crusting and oozing can follow.
- Asteatotic eczema is eczema due to dry skin or xerosis. The typical presentation is scaling of the lower extremities in the elderly.

INVESTIGATION

- Diagnosis is clinical.

TREATMENT

Goal of treatment

- To help heal dry skin, prevent its return and reduce discomfort

Non pharmacologic:

- Avoid excessive bathing
- avoid strong alkaline harsh soaps
- liberal application of emollients

Pharmacologic:

- Topical steroids are not helpful unless there is severe pruritus and severe inflammation.

18.3 ITCHING

BRIEF DESCRIPTION

- Pruritis is defined as unpleasant sensation that provokes the desire to scratch.
- Itching is a symptom that can cause significant discomfort and is one of the most common reasons for consultation with a dermatologist.
- Pruritus with skin rash can occur as a result of dermatological disorders (e.g.: xerosis, atopic dermatitis, contact dermatitis, fungal skin infections)

or less commonly, a systemic disease (e.g.: allergic reactions, cholestasis, chronic kidney disease like hematologic malignancy, thyroid disorder, diabetes mellitus, lymphoma and psychiatric disorders.).

- Also, drugs can cause itching (e.g., morphine, some IV contrast agents)

DIAGNOSIS

- A detailed history and physical examination are key for proper diagnosis. Lab investigations such as CBC, liver, renal, and thyroid function measurements and appropriate evaluation for underlying cancer are important when a systemic disorder is suspected.

TREATMENT

- Any underlying disorder should be treated. Supportive treatment involves
  - local skin care: lukewarm bathing, frequent lubrication and avoidance of irritating or tight clothing
  - topical treatment: options include lotions or creams that contain camphor and/or menthol, capsaicin or corticosteroids.
- Systemic treatment: oral antihistamines such as diphenhydramine 25-50mg P.O., QD or, chlorpheniramine4-6mg P.O., QD or cetirizine 10mg P.O., QD for 7 to 10 days.

18.4 ACNE VULGARIS

BRIEF DESCRIPTION

- Acne vulgaris is a chronic inflammatory disease of the pilosebaceous follicles.
- It can occur at any age, but it is most common during adolescence.
- The main pathology is overproduction and excessive accumulation of sebum due to blockage of its flow into the surface of the skin.
- The disease is characterized by a great variety of clinical manifestations, non-inflammatory or inflammatory.

CLINICAL FEATURES

- Comedones (black or white heads).
- Papules, pustules, nodules, cysts or scars.
- Lesions are mostly confined to the face, upper arm, chest and back.

INVESTIGATIONS

- Diagnosis is clinical.
- Acne is classified into mild, moderate and severe depending on severity.
    - Mild acne: comedons and few papules
    - Moderate acne: multiple papules and few nodules
    - Severe acne: multiple nodules, cysts and scars.

TREATMENT

Goal of treatment

- Improve cosmetic appearance
- Prevent complications particularly the development of scars that can lead to permanent disfigurement.

Non pharmacologic

- Cleansing the face with oil-free cleansers twice daily
- Avoiding picking and squeezing acne lesions
- Avoiding oily cosmetics, moisturizers and Vaseline
- Use oil free moisturizers and alcohol containing toners.
- Educating patients that treatment results are slow and counseling of patient.

Pharmacologic

Mild Acne: First line

- **Retinoic acid (Tretinoin)** – start with 0.025% cream or 0.01% gel and gradually increase the concentration if there is no improvement to 0.05% cream or 0.025% gel, then to 0.1% cream, then to 0.05% lotion.

- Start with every other day regimen and make twice daily based on tolerance of the skin for irritating effect of retinoids. Improvement is seen after 2–5 months.

Alternatives

- **Salicylic acid** 2-3%gel, cream or lotion
- **Clindamycin**, 1% gel or lotion;
- **Erythromycin** 2-4% gel, lotion or cream,
- **Azelaic Acid** 20% applied twice daily.

Moderate Acne

First line

- The above topical medications

  PLUS

- **Doxycycline**, 100mg P.O., QD for 3 to 6 months depending on clinical response

  OR

- **Tetracycline**, 250-500mg two to four times daily for three to six months.

  OR

Severe Acne

- Refer the patient to dermatology center.

18.5 BACTERIAL INFECTIONS OF THE SKIN AND SOFT TISSUE

BRIEF DESCRIPTION

- Common bacterial skin infections include cellulitis, erysipelas, impetigo, folliculitis, furuncle and carbuncles.

CELLULITIS AND ERYSIPELAS

- Cellulitis and erysipelas are a diffuse inflammation of the subcutaneous tissue and the skin due to bacterial infections.
- Cellulitis usually occurs through a breach in the skin surface especially if tissue edema is present, but may abruptly affect normal skin.
- It is usually caused by Streptococcus pyogenes and also caused by staphylococcus aureus especially in the presence of trauma. But other bacteria such as Haemophilus influenza and gram–negative organisms can cause cellulitis especially in children.
- Erysipelas is a more superficial form and is usually due to group A streptococci.

CLINICAL FEATURES

- Fever and malaise
- Warmth, redness, tenderness of the affected site: lesion of erysipelas is well demarcated and more erythematous than cellulitis
- Swelling of affected site which is more prominent in cellulitis than erysipelas
- Enlarged and tender regional lymph nodes

INVESTIGATIONS

- CBC
- Fasting blood glucose.
- Wound swab for culture and sensitivity, if there is pus
- Blood culture (in the seriously ill).

TREATMENT

Goal of treatment

- Relieve pain.
- Control the infection

- Treat predisposing infection/s.

Non pharmacologic

- Bed rest
- Application of warm compresses
- Elevation of an affected limb.

Pharmacologic

- Patients with mild cases of cellulitis usually treated on an outpatient basis with beta-lactam antibiotics:

First line

- **Cloxacillin** 0.5 – 1gm every 4 hrs should be administered intravenously until the fever subsides, (usually 2 – 3 days). Then **Cloxacillin** 500 mg. P.O QID should be continued for 7 days.
- Presence of severe systemic symptoms is an indication for hospital admission and patients should be treated with **Crystalline Penicillin** 1.2-2.4 million units IV 4 hourly.

Alternative

- **Cephalexin** 500 mg PO TID for 7 days
- **Erythromycin** 500 mg PO QID for 10 days

N.B. In all children with facial or periorbital cellulitis, coverage for *Haemophilus* should be provided with **Chloramphenicol** 30 to 50mg/kg/d divided in two four doses

- **Cephalexin**, **500 mg P.O., QID** or
- **Amoxicillin** 500 mg P.O., TID
- **Cloxacillin** 500 mg P.O., QID

CARBUNCLES AND FURUNCLES

- Furuncle is a single deep-seated infectious folliculitis and perifolliculitiis with a purulent core by staphylococcus aureus.

- When multiple adjacent furuncles are involved with deeper communicating lesion it is called carbuncle.
- It affects mainly young men who are otherwise healthy but patients must be evaluated for predisposing factors: alcoholism, medicine abuse, diabetes mellitus, leukemia and other malignancies, AIDS and chronic liver disease.

CLINICAL FEATURES

- Fever, Pain, swelling and erythema of the involved area.
- Painful smooth dome shaped lesions that increase in size followed by suppuration in 5-7 days and pus discharge through multiple orifices.
- Any area of the skin may be affected but common areas include face, neck, axilla, chest, back, hip and thigh.

INVESTIGATIONS

- Gram stain and culture of pus for carbuncle

TREATMENT

Goal of treatment

- Eradication of the infection.
- Minimize scarring

Non pharmacologic

- Accumulation of pus (abscess) should be incised and drained in addition to oral antibiotic
- Bed rest for patients with systemic symptoms, impaired immunity and with involvement of the face

Pharmacologic

- For simple superficial bacterial folliculitis topical treatment with or fusidic acid applied twice daily for 7 days is effective.
- Systemic therapy is required for furunculosis of the face or when generalized symptoms or impairment of the immune system are present.

- Penicillinase resistant antibiotics like Cloxicillin or dicloxicillin are preferable.

First line

- **Cloxicillin**

Children; 50 – 100mg/kg /day P.O., for 7 to 10 days divided into four doses

Adults; 500mg P.O, QID for 7- 10 days.

Alternatives

- **Erythromycin**,

Children; 30–50mg/kg/day for 7 to 10 days in 4 divided doses

Adults; 500mg P.O, QID for 7 -10 days.

OR

- **Cephalexin**,

Children; 25 to 100mg/kg in 4 divided doses for 7-10 days.

Adults; 250 to 500mg QID for 7 - 10 days.

Impetigo

BRIEF DESCRIPTION

- Impetigo is a contagious superficial infection of the skin that is caused by Streptococci or
- Staphylococci or by both organisms. Infection is acquired either from external sources by direct contact or through objects or from internal infection, e.g. nasopharyngeal sources.
- Impetigo contagiosa is highly infectious and is common in children. it is commonly associated with poor hygiene and crowded living conditions
- There are two forms; non-bullous impetigo and bullous impetigo.

CLINICAL FEATURES

- Non-bullous impetigo-lesions are thick, adherent and recurrent dirty yellow crusts with an erythematous margin.

- Bullous impetigo is caused by Stap. aureus and non-bullous impetigo is caused by group a beta-hemolytic streptococcus.
- Bullous impetigo characterized by superficially thin-walled bullous lesions that rupture and develop thin, transparent, varnish like crust.

INVESTIGATIONS

- Microscopy and culture of the exudates from the blisters (not routinely required except in recurrent cases)

TREATMENT

Goal of treatment

- Treat infection.
- Break the cycle of transmission.

Non pharmacologic

- Local treatment is by careful removal of crusts by cleaning with Normal saline or Hydrogen peroxide for more rapid healing.

Pharmacologic

Topical: for localized

First line

- **Mupirocin**, applied thin film of 2% cream/ointment 2-3 times a day for 10 days.

Alternatives

- **Gentian violet** 0.5 % for 10 days
- **Fusidic acid**, applied thin film of 2% cream 2-3 times in a day for 10 days.

N.B. Anti-bacterial ointments are usually applied after the wet lesion has dried.

Systemic: for extensive cases

First line

- **Cloxacillin** 500 mg PO QID for 7 to 10 days.

Alternative

- **Cephalexin**, 250mg to 500mg P.O., QID for 7 to 10 days for adults; 25 to 100mg/kg

P.O. in 4 divided doses for 7 to 10 days for children

Chronic lower limb ulcers

Brief description

- Ecthyma is a term that describes ulcers forming under a crusted surface infection. It is an ulcerative deeper tissue infection, especially of the lower extremities in which the lesions extend through the epidermis and deep into the dermis.
- It can occur when impetigo is neglected.
- It is caused by group A streptococcus. Concomitant staph. aureus infection is common.
- More wide spread infection, permanent scarring and rarely post streptococcal glomerulonephritis are some of the complications of Ecthyma

Clinical features

- It presents as deep punched ulcers that are covered by dirty grayish-yellow crust on the lower extremities.

Investigation

- Diagnosis is clinical: the crust should be removed to see the ulcer

Treatment

Goal of treatment

- Eradication of the infection.
- Minimize scarring

Non pharmacologic

- Would debridement
- Regular cleansing with antiseptics

Pharmacologic

- Topical antibiotic ointment such as fusidic acid or mupirocin
- **Erythromycin 500mg** P.O., QID for six weeks

Alternative

- **Cloxacillin or Cephalexin** can also be used as alternatives for severe and extensive cases
- N.B: ecthyma gangrenosum is an uncommon type of ecthyma that is caused by pseudomonas aeruginosa.Aggressive surgical debridement with antipseudomonal drugs such as fluoroquinolones and aminoglycosides are necessary.

NECROTIZING FASCIITIS AND PYOMYOSITIS

BRIEF DESCRIPTION

- Necrotizing fasciitis is a rapidly progressive inflammatory infection of the fascia with secondary necrosis of the subcutaneous tissues.
- A mixture of pathogens, usually including streptococci and anaerobes, is responsible for this rare condition. pyomyositis is purulent infection of skeletal muscle that arises from hematogenous spread, usually with abscess formation.
- It most commonly affects the muscles of the limbs and torso. risk factor for necrotizing fasciitis and pyomyositis include surgical procedures, trauma, minor insect bite, chronic illness such as DM and liver cirrhosis and immunocompromised states.

CLINICAL FEATURES

- Intense pain and tenderness over the involved skin and underlying muscle. other findings may include skin vesicles, crepitus and edema extending beyond the area of erythema can be signs of necrotizing fasciitis

- Pyomyositis presents with fever and pain with cramping localized to a single muscle group. Quadriceps muscle is the most commonly involved muscle
- Patients can present with variable sign and symptoms and can present at different stage of the disease.

INVESTIGATION

- **Lab:** CBC, ESR, OFT, electrolyte, blood and tissues cultures, creatine kinase, aspiration and gram stain
- **Radiographic imaging:** x ray, CT scan, MRI, Doppler ultrasound

surgical exploration is the definite way to establish the diagnosis of necrotizing infection and distinguish it from other entities.

TREATMENT

- Since Necrotizing fasciitis is a surgical emergency, the patient should be admitted and surgical debridement and antibiotic therapy is initiated.possible regimens include combination of **penicillin G and aminoglycosides** as well as clindamycin.
- Pyomyositis - few patients can be treated with antibiotics alone. but patients presenting with advanced stages need both antibiotics and drainage for definitive management.

18.6 FUNGAL INFECTIONS OF THE SKIN

CANDIDIASIS (MUCOCUTANEOUS CANDIDIASIS)

- Candidiasis is an infection caused by the yeast like fungus Candida Albicans. Infection by this fungus may cause different types of lesions on the skin, nail, mucous membrane and viscera.
- The areas where warmth, and maceration of the skin permit the organism to thrive, are frequently affected. These are the perianal and inguinal folds, the interdigital areas and the axillae.

- It may be a normal inhabitant at various sites until there is some change in the state of the area, and then it becomes a pathogen.
- Abnormal moisture also promotes its growth, as in moist lip corner.
- **Clinical features** and **investigations** depend on each specific site.

BALANOPOSTHITIS

- **Balanoposthitis** refers to candida infection of the penis.

CLINICAL FEATURES

- Small papules or fragile papulopustules on the glans or in the coronal sulcus

INVESTIGATIONS

- Microscopic examination after KOH preparation

TREATMENT

Objectives

- Eradicate infection

Non pharmacologic

- Manage predisposing factors like maceration and underlying diseases like diabetes and immunosuppression.

Pharmacologic

First line

- **Clotrimazole**, thin film of 1% cream applied to the lesion BID for about 2-3 weeks

Alternative

- **Miconazole**, thin film of 2% cream applied to the lesion bid for about 2-3 weeks.

Candidal Intertrigo

- Usually involves the great folds of the body (groin, inframammary, axillae, scrotum, perianal areas). It also affects the area between the fingers and toes.

CLINICAL FEATURES

- Red, oozing band with a whitish macerated center and a scaly border at the affected fold.
- Isolated, flaccid, satellite, vesiculo-pustules which, when they break, show collar of scale at the periphery.

INVESTIGATIONS

- Microscopic examination after KOH preparation

TREATMENT

Objectives

- Eradicate infection
- In those suffering from diabetes mellitus, treatment consists of bringing the diabetes under control.

Non pharmacologic

- Avoidance of chronic exposure to moisture.

Pharmacologic

- Topical application of, **Clotrimazole, Miconazole**

CANDIDAL PARONYCHIA

BRIEF DESCRIPTION

- Chronic inflammation of the nail fold.
- This type of infection is usually caused by *C.albicans* but Acute paronychia is caused by staph. Aureus.
- Chronic paronychia is often seen individuals whose hands are constantly wet as a result of their occupation and in elderly diabetics.

CLINICAL FEATURES

- Chronic paronychia causes redness, swelling, and pain of the tissue around the nail.
- Pressure on the affected region may elicit a malodorous pus.
- In chronic paronychia, the cuticle separates from the nail plate, leaving the region between the proximal nail fold and the nail plate vulnerable to infection.
- It can be the result of dish washing, finger sucking, aggressively trimming the cuticles, or frequent contact with chemicals.

INVESTIGATIONS

- Microscopic examination after KOH preparation

TREATMENT

Objectives

- Eradicate infection

Non pharmacologic

- Avoidance of chronic exposure to moisture is an important prophylactic measure.

Pharmacologic

- Topical application of, **Clotrimazole, Miconazole cream apply BID**

OR

- **Systemic treatment with**

First line

- Fluconazole 200 to 400mg PO once weekly for 10 weeks.

Alternatives

- **Itraconazole**, pulse dosing with 200mg BID for 1 weak of each of 3 consecutive months.

GENITAL CANDIDIASIS (VULVOVAGINITIS)

- Refer Gynecology section

ORAL CANDIDIASIS (THRUSH)

BRIEF DESCRIPTION

- Oral thrush are thick white plaques that adhere to the oral mucosa with moist, reddish, and macerated base.
- It can be a sign of immunosuppression and dry mouth can be the predisposing factor, because saliva inhibits growth of candida.

CLINICAL FEATURES

- Pseudomembranous form- The most common form characterized by white plaques on the buccal mucosa, palate, tongue or oropharynx.
- Atrophic from- Commonly found under dentures and characterized by erythema without plaques.

INVESTIGATIONS

- Microscopic examinations of KOH preparations of the scrapings of the white patches or erosive areas of the mucosa.

TREATMENT

Objective

- Eradicate Infection

Non-pharmacologic

- Manage predisposing factors like maceration and underlying diseases like diabetes and immunosuppression.

Pharmacologic

- Topical application of **Clotrimazole** or **Miconazole** or **Nystatin** for 15 days

OR

- Systemic treatment with loading dose of **Fluconazole** 200mg PO and maintenance dose of 100/200mg PO/day for 7-14 days *OR* **Itraconazole** 200mg PO/day for 05-10 days OR

Dermatophytoses (ring worm)

- Superficial fungal infections (**Dermatophytoses**) usually affect all parts of the skin from head to toes. These include:
  - Infection of the scalp- Tinea capitis
  - Infection of the skin of the trunk and extremities- Tinea corporis
  - Infection of the axillae or groin- Tinea cruris
  - Infection of the nails- Tinea unguium (Onychomycosis)Infection of the hand - Tinea manuum
  - Infection of the foot - tinea pedis
  - Infection of the beard area - Tinea babae
  - Infection of the face - Tinea faciei
  - Infection of the palms and soles- Tinea interdigitalis

TINEA CAPITIS

- It is a fungal infection of the scalp that most often presents with pruritic, scaling areas of hair loss.
- The major causes are Trichophyton and Microsporium species of dermatophyte fungi. Infection is acquired by direct contact with another human or animal or soil.
- It primarily occurs in children between the age group of 2 to 14 years of age.

CLINICAL FEATURES

- There are five major clinical variants with pruritus as a common associated symptom.
  - Scaly gray patches with alopecia

  - Patches of alopecia with black dots
  - Kerion
  - Favus

Investigation

- Microscopic examination of KOH preparations of the proximal ends of the plucked hair or scraps from scalp lesions.

Treatment

Nonpharmacologic

- Good hygiene

Pharmacologic

Systemic antifungals

First Line

- **Griseofulvin** 20 to 25mg/kg /day for 6 to 8 weeks

Alternative

- First Line- **Terbinafine**
- Other Alternatives- Fluconazole or **Itraconazole.**
- Adjunctive Intervention- Shampoo with antifungal properties. (Selenium Sulfide 1 or 2.5 %, or Ketoconazole 2% shampoo) at least twice weekly.

TINEA CORPORIS

- It is a cutaneous dermatophyte infection occurring in sites other than feet, groin, face or hand. The major causes are Trichophyton and Microsporium species of dermatophyte fungi. Infection is acquired by direct skin contact with another human or animal.

CLINICAL FEATURES

- Pruritic, circular or oval, erythematous, scaling patch or plaque that spreads centrifugally.

INVESTIGATION

- Microscopic Examination of KOH preparations of skin scrapings from the active border of plaque.

TREATMENT

- Topical Antifungal- **Clotrimazole, Miconazole or ketoconazole** or terbinafine cream (Dosage described below)
- Systemic Antifungal may be alternative for patients with extensive skin involvement or failed topical therapy. - **Terbinafine** 250mg PO/day for 1-2 weeks, **Itraconazole** 200mg PO/day for 1 week, **Fluconazole** 150 to 200mg once weekly for 2-4 weeks.

TINEA PEDIS (ATHLETE'S FOOT)

BRIEF DESCRIPTION

- Is the most common dermatophyte infection. It may manifest as an interdigital (usually), hyperkeratotic, or vesiculobullous eruption and rarely as ulcerative skin disorder.
- It usually occurs in adults and adolescents particularly in young men and is rare before puberty.
- It is usually caused by Trichophyton and Epidermophyton species.
- Infection is acquired by means of direct contact with the causative organism during barefoot or walking bare foot especially in shower rooms, sharing socks, shoes with infected person.

CLINICAL FEATURES

- Interdigital- Commonly manifests as pruritic, erythematous erosions or scales between the toes, especially in the third and fourth digital interspaces.
- Mucasin – commonly manifest as hyperkeratotic scaling on the soles.
- Vesiculobullous- commonly manifest as vesicular or bullous lesion on the sole of the foot.

INVESTIGATION

- Microscopic examination of KOH preparations from skin scrapings of affected area.

TREATMENT

Objective

- Alleviate pruritus,
- Reduce risk for secondary bacterial infection,
- Limit spread to other body sites or other individuals.

Topical antifungals

- First line treatment- **Clotrimazole, Miconazole or ketoconazole**

Systemic antifungal

- Reserved for failed topical therapy.
- **Terbinafine** 250mg PO/day for 2 weeks, OR
- **Itraconazole** 200mg PO/day for 1 week, OR
- **Fluconazole** 150 to 200mg once weekly for 2 to 6 weeks.

TINEA UNGUIUM

BRIEF DESCRIPTION

- Is infection of the nail plate. T. Rubrum is the most common cause but it can be caused by other species of trichophyton and microsporium species.

CLINICAL FEATURES

- Distal lateral subungual onychomycosis- Is the most common clinical subtype. It presents with whitish, yellowish or brownish discoloration of a distal corner of a nail.
- White Superficial onychomycosis- It is characterized by dull white spots on the surface of the nail plate.
- Proximal Sublingual onychomycosis
- Endonyx onychomycosis- It only involves the interior of the nail plate

sparing the nail bed.

- Total dystrophic onychomycosis- Describes complete destruction of the mail plate.
- Mixed pattern Onychomycosis

INVESTIGATION

- Microscopic Examination of KOH preparations

TREATMENT

- Topical antifungals /Systemic antifungals are the mainstay of treatment.
- Terbinafine, if the patient weighs 20 to 40kg the dose is 125 mg po once daily for 6 to 12 weeks or if the patient weighs above 40 kg the dose is 250 mg po once daily for 6 to 12 weeks.
- Fluconazole 200 to 400 mg po once weekly for 12 weeks in case of finger nail infection.

GENERAL TREATMENT FOR DERMATOPHYTOSIS.

Non pharmacologic

- Good basic hygiene
- Use of loose clothing

Topical First Line

- **Clotrimazole**, thin film of 1% cream applied BID for 2-3 weeks.

OR

- **Ketoconazole**, thin film of 2% cream applied BID until the infection clears (usually for 2-3 weeks)

OR

- **Miconazole** thin film of 2% cream applied BID until the infection clears (usually for 2-3 weeks).

PITYRIASIS VERSICOLOR (PV)

Brief description

- PV is a chronic asymptomatic scaling dermatosis associated with the overgrowth of the hyphal form of Pityrosporum ovale, Malassezia furfur.
- It is a common disorder seen in older children and adolescents around puberty.
- The lesions sometimes may involve other areas such as the abdomen, upper arms, thighs and face.
- The disorder is insidious in onset and persistent. After successful treatment recurrences are common.

CLINICAL FEATURES

- Well demarcated scaling patches with variable pigmentation. Most commonly seen on the trunk.

INVESTIGATIONS

- KOH preparation and culture

TREATMENT

Objectives

- Eradicate infection
- Prevent transmission

Non pharmacologic

- Good personal hygiene
- Avoid sharing bath towels, sponges and clothing

PHARMACOLOGIC

Topical imidazole

- **Clotrimazole, Miconazole** and **Ketoconazole** cream can be applied once or twice daily for four to six weeks.

- **Ketoconazole** shampoo can also be used to wash and left for 10 minutes to the affected areas daily for a period of 7 days.
- Similarly, 2.5% **selenium sulfide shampoo** can be used.

Systemic therapy:

- In cases with extensive and long-standing eruptions one of the following regimens can be used.

First line

- **Ketoconazole**, 400mg single dose, repeated after a week. OR 200mg daily or 3-4 mg/kg/day for 7-14 days

Alternative

- **Fluconazole**, 400mg single dose, repeated after a week.

  OR

- **Itraconazole**, 400mg P.O., single dose OR 200mg P.O., BID on first day, then 200mg P.O., daily for 5 days.

SECONDARY PROPHYLAXIS

- **Selenium sulfide** or **ketoconazole** shampoo once or twice a week
- **Salicylic acid/sulfur bar, zinc pyrithione** (bar or shampoo) can be used weekly.

18.7 EXO-PARASITIC INFESTATION

LICE: BODY AND HEAD LICE

BRIEF DESCRIPTION

- Lice infestation or pediculosis is a common disorder due to lice infestations.
- Lice are Ectoparasite that live on or near the body and usually die within 10 days of removal from their human host.
- Pediculosis is caused by Human Ectoparasite: Pediculus humanus corporis-

the body louse-and Pediculosis humanus capitis-the head louse.

- Contact with an infected individual, poor hygiene and living in crowded areas such as homeless shelters are major risk factors and contribute to this disease.
- Sites of predilections are shoulders, trunks and buttocks.
- Untreated cases may persist indefinitely.
- Bacterial infection is a typical complication in neglected cases.

CLINICAL FEATURES

- Pruririts is usually the chief complaint and hallmark of lice infestation.
- Head lice are associated with excoriated lesions that appear on the scalp, ears, neck and back.
- The primary bite lesion is a small red macule, or occasionally a papule with a characteristic central hemorrhagic punctum.

Investigation

- Diagnosis is clinical

TREATMENT

Goal of treatment

- Eradicate the parasite from clothing.

Non pharmacologic

- Boil clothes with hot water or iron the clothes after washing with cold water
- Nits should be removed using fine comb. Shaving is also recommended

Pharmacologic

First Line

- **Malathion shampoo** applied to the scalp and left for 2 hours before rinsing.

- **Permethrin lotion or shampoo,** applied on the scalp for 10 minutes and washed off

SCABIES

BRIEF DESCRIPTION

- Scabies is a very common infestation characterized by persistent and intensely itchy skin eruption due to the mite Sarcoptes scabies.
- The disease is commonly seen in people with low socio-economic status and spreads through intimate personal contact, facilitated by overcrowding and poor hygiene.

CLINICAL FEATURES

- Red papules and burrows in the axilla, groin and digital web spaces associated with complaints of nocturnal pruritus.
- diffuse excoriations, lichenifications, eczematizations and secondary infections can also be seen.
- In infants, the face, palms and soles are often involved and blisters may develop.

TREATMENT

Goal of treatment

- Eradicate the mite
- Prevent transmission to family members and close contacts

Non pharmacologic

- Putting the clothing used by the infected individual(s), including bedding and mattresses in the sun.
- washing clothes in hot water or ironing clothes after normal washing

Pharmacologic

Topical:

First line

- **Permethrin 5%,** Thin films of cream applied to all areas of body from the neck down
- And is washed off after 8-14 hours. Repeat the same dose after a week

Alternative

- **Benzyl benzoate,** applied to the entire body, neck to toe for 3 to 5 consecutive evenings. Bath should be taken before the first and after the last application.
- **Sulphur ointment**, Children 5%, Adult 10%: thinly applied twice daily to the entire body for 3 consecutive nights. The patient should wash thoroughly before each new application and 24 hours after the last treatment.

SYSTEMIC:

- **Ivermectin**, 200µg/kg as a single dose, for Norwegian (crusted scabies) and resistant forms of scabies. And it is ideal for institutional outbreaks.
- Antihistamines are given for pruritus and antibiotics such as Cloxicillin are given for bacterial super infection.

N.B. Any person who has had close contact with the infected patient should be treated.

Alternatives

- **Dapsone**, 50-100 mg P.O, daily
- **Spironolactone**, 50–100 mg daily for up to six months
- **Combined oral contraceptive pill** for women for up to six months.
- **Intralesional Triamcinolone acetonide** 40mg per ml diluted with equal amount of Normal saline or local anesthesia repeated every four weeks is effective for few nodules, cysts or hypertrophied acne scars.

18.8 VIRAL SKIN DISORDERS

HERPES SIMPLEX (HS)

BRIEF DESCRIPTION

- HSV is a double-stranded DNA virus that exists as two separate types (type 1 and 2) .it belongs to the family Herpesviridae.
- Herpes simplex infection can involve the skin, mucosa, eyes and central nervous system. it establishes a latent state followed by viral reactivation and recurrent local disease.
- The skin lesion is characterized by painful grouped micro vesicles which soon rupture to form yellow crust.
- Infection with H.S. virus is so common in man as to be regarded as almost universal and antibodies can be demonstrated in the plasma of virtually in over 85% of the adult population.
- Transmission is usually skin to skin, skin to mucosa and mucosa to mucosa. A fetus may be infected in utero. It is caused by Herpes virus hominis.

CLINICAL FEATURES

- itching, tingling or burning sensation usually precedes skin lesions
- Painful grouped vesicles or blisters.
- Fever, malaise and headache.

INVESTIGATIONS

- Diagnosis is clinical.
- Doubtful cases and non-typical cases should be confirmed with laboratory testing: PCR, viral culture, antigen detection or Tzanck smear,

TREATMENT

Goal of treatment

- Relieve pain and discomfort

- Limit extent of disease spread in the immunocompromised and atopic eczema patients
- Prevent secondary infection

Non pharmacologic

- No specific measure

Pharmacologic

- No specific treatment for herpes labialis which is usually self-limiting
- **Acyclovir**, 200mg PO five times daily OR 400mg P.O three time daily for 5- 7 days

Children <2 years; half adult dose.

Children >2 years; adult dose.

- **Paracetamol** for pain

Prevention

- Practicing safe sex and barrier protection using latex condoms helps to minimize exposure to genital HSV infections.

HERPES ZOSTER

BRIEF DESCRIPTION

- Herpes zoster or shingles is an acute dermatomal infection characterized by a painful, usually vesicular eruptions.
- A latent infection in sensory dorsal root ganglia is caused by VZV, and the reactivation of this latent VZV infection results in herpes zoster.
- Older age, immunocompromised state, chronic diseases and autoimmune diseases are some of the risk factors.

CLINICAL FEATURES

- A deep stabbing, burning or penetrating pain is the most common first symptom usually preceding the eruption

- Eruptions of papules that quickly changes to become vesicles or bullae which evolve into pustules, crusts or hemorrhagic lesions within few days.
- Fever, headache, malaise and fatigue
- Post herpetic neuralgia: a shooting and persistent pain that occurs after skin lesions have healed.

INVESTIGATIONS

- Diagnosis is clinical.

Treatment

Goal of treatment

- speed up the resolution of the acute viral infection
- Relieve pain and discomfort
- Prevention of post herpetic neuralgia (PHN)

Non pharmacologic

- No specific measure.

Pharmacologic

- Acyclovir, 800 mg PO five times daily for 7-10 days. It should be started as early as possible
- Pain should be treated aggressively with nonprescription analgesics or narcotics.
- Amitriptyline, 75 mg PO at bedtime with or without Carbamazepine 400 mg or
- Gabapentin started with 300 mg PO daily and gradually increasing to 300-600 mg PO TID is helpful for patients with PHN

MOLLUSCUM CONTAGIOSUM

BRIEF DESCRIPTION

- Molluscum Contagiosum is a disease caused by molluscum contagiosum virus (MCV) a member of the poxvirus family.

- It is seen most commonly in children but can also be transmitted sexually among adults.
- It is associated with immunodeficient stats such as HIV infection

CLINICAL FEATURES

- It is asymptomatic unless superinfected
- The typical lesion is a pearly, skin colored papule with central umbilication

INVESTIGATIONS

- Diagnosis is clinical

TREATMENT

Goals of treatment

- Prevent autoinoculation and transmission to close contacts and sexual partners.

Non pharmacologic

- **Surgical**: curettage, cryosurgery and electro surgery for selected cases

Pharmacologic

- Treatment is usually not medically mandatory as the infection is self-limited and spontaneously resolves after few months.

First line

- **KOH 5-10% solution**, first apply Vaseline to perilesional area (to avoid normal skin irritation) then applied over the lesion with cotton tip applicator daily

OR

- **Iodine**, applied 2-3 times per week by unroofing the top of the lesion and the procedure is continued until the lesions disappear (1-2 weeks).

Alternative

- **Retinoic acid (Tretinoin)**, thin films applied to the lesion daily OR,
- **Silver Nitrate 40% paste**

N.B. Therapy based on physical removal of the lesions is considered best. Sexual partners should also be examined and treated. Treatment is aimed at removal of the lesions or at least the central core of each lesion. This is thought to initiate the lost immune response via injury to the epidermis and release of viral antigens.

PITYRIASIS ROSEA

BRIEF DESCRIPTION

- Pityriasis rosea is a common, self-limited skin condition with a distinctive morphology mainly affecting children and adults.
- The cause of pityriasis is unknown but a viral etiology such as human herpes virus 6 and 7 has been proposed.

CLINICAL FEATURES

- The eruption starts as a solitary, oval plaque with scaling at the border and is called the herald patch. It is followed by smaller lesions appearing on the trunk and extremities.
- Itching may be present

INVESTIGATION

- Diagnosis is clinical

TREATMENT

Goal of treatment

- Relieve symptoms
- Treatment is not usually required other than reassurance that it will resolve on its own over weeks.
- Topical steroids, topical calamine and antihistamines may be used to relieve itching when there is pruritus involved

18.9 DRUG REACTIONS AND ALLERGIES

- Adverse cutaneous drug reactions are common in hospitalized (2–3%) as well as in ambulatory patients (>1%).
- Most reactions are mild, accompanied by pruritus and resolve promptly after the offending drug is discontinued.
- Severe, life-threatening ACDRs do occur and are unpredictable.
- Must be the first consideration in the differential diagnosis of a suddenly appearing eruption.
- They are caused by immunologic or nonimmunologic mechanisms.
- The majorities are based on a hypersensitivity mechanism

STEVEN JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN)

- An acute life-threatening severe Mucocutaneous reactions
- Characterized by extensive necrosis and detachment of the epidermis leading to vesico-bullous lesions involving the skin and mucous membranes.
- Mucous membranes are affected in over 90 percent of patients, usually at two or more distinct sites (ocular, oral, and genital).
- Medications are the leading trigger of SJS/TEN
- Allopurinol, lamotrigine, aromatic anticonvulsants, antibacterial sulfonamides, and “oxicam” or COX-2 inhibitor Nonsteroidal anti-inflammatory drugs (NSAIDS) are most commonly implicated.
- Mycoplasma pneumonia infection is the next most common trigger of SJS/TEN.

CLINICAL FEATURES

Symptoms

- A suggestive history of drug exposure or febrile illness.

- Time from first drug exposure to onset of symptoms: 1–4 weeks.
- Occurs more rapidly with rechallenge.
- Prodromes: fever, malaise, arthralgia 1–3 days prior to mucocutaneous lesions.
- A painful rash that progresses rapidly.

Signs

- Start as a red morbilliform rash
- Purple skin necrosis and blisters
- Positive Nikolsky sign and/or "bulla spread sign."
- Oral, ocular, and/or genital mucositis with painful mucosal erosions.
- Necrosis and sloughing of the epidermis of varying degree
- Mucous membrane erosions are common and internal organ involvement may be present
- The extent of epidermal detachments should be estimated and recorded as the percentage of the body surface area (BSA) involved.
- SJS when BSA involvement is less than 10%.
- SJS –TEN overlap 10-30 % BSA involvement
- TEN when more than 30 % of BSA affected.

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis is based upon clinical findings in a patient with a history of antecedent drug exposure or febrile illness.
- Histologic findings on skin biopsy may be supportive but not independently diagnostic.
- Culture when there is evidence of infection
- Follow electrolytes and RFT in more extensive lesions

TREATMENT

GOAL OF TREATMENT

- Early recognition and stop offending drug
- Supportive care
- Good nursing care
- Prevention of dehydration and sepsis
- Patients usually require care

PHARMACOLOGIC

Corticosteroids

- The role of using systemic corticosteroids is uncertain. However, systemic steroid 1mg/kg/day as adjunctive therapy early in the course of the disease (ie, within 24 to 48 hours of symptom onset) may be considered.
- Using cyclosporine 3 to 5 mg/kg/day as adjunctive therapy early in the course of the disease (i.e., within 24 to 48 hours of symptom onset) may be considered

Antibiotic therapy

- Systemic antibiotics may be indicated, depending on results of appropriate cultures.

Non-pharmacologic

- Should be managed as burn patients, if possible, should be admitted to burn unit.

DRESSINGS

- Skin hygiene; daily cleansing and bland, non-adherent dressings as needed.
- Do not use silver sulfadiazine if condition is thought to be due to cotrimoxazole or other sulphonamide.
- Surgical debridement not recommended.
- Infection control measures are crucial

MUCOUS MEMBRANES

- Regular supervised oral, genital and eye care to prevent adhesions and scarring.
- With oropharyngeal involvement, suction frequently to prevent aspiration pneumonitis.

FLUIDS

- Oral rehydration is preferred but intravenous fluid therapy may be required in significant dehydration.
- Encourage oral fluids to prevent pharyngeal adhesions
- Provide soft, lukewarm food or nasogastric feeds if unable to eat.

PREVENTION

- The patient Should be given paper with documentation of the offending agent and others with possible cross reaction
- These drugs must never be readministered.
- It should be documented on the chart in bold

DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)

BRIEF DESCRIPTION:

- Also called Drug-Induced Hypersensitivity Syndrome (DIHS)
- It is a severe idiosyncratic reaction characterized by fever (38 to 40°C), malaise, lymphadenopathy, and skin eruption.
- Additional systemic symptoms may be related to visceral involvement (e.g., liver, kidney, and lung).
- The aromatic antiepileptic agents (carbamazepine, phenytoin, lamotrigine, and phenobarbital), allopurinol, and the sulfonamides are the most frequent causes of this disorder.

CLINICAL FEATURES:

Symptoms

- Begins two to six weeks after the initiation of the offending medication.
- Fever (38 to 40°C), malaise, lymphadenopathy, and skin eruption are the most common initial symptoms, but they are not invariably present.
- Systemic symptoms include fever (38 to 40°C [100.4 to 104°F]), malaise, lymphadenopathy, and symptoms related to visceral involvement.

Signs:

- A morbilliform eruption that progresses more or less rapidly to a diffuse, confluent, and infiltrated erythema with follicular accentuation.
- The face and upper part of the trunk and extremities are involved initially.
- Diffuse lymphadenopathy will be there in 30 to 60 percent of cases.

INVESTIGATIONS AND DIAGNOSIS:

- CBC (Leukocytosis with eosinophil counts >700)
- Liver enzymes and renal function test
- Skin biopsy (an interface dermatitis and a perivascular infiltrate of lymphocytes and eosinophil's)
- Diagnosis is clinical

TREATMENT

Goal of treatment

- Stop (or substitute) all suspect medications and discontinue non-essential medications
- Identify patients with severe organ involvement.

Non-pharmacologic

- Identification and prompt withdrawal of the offending drug

- Serial biochemical measurements should be performed to monitor liver function in patients with liver injury

Pharmacologic

- Topical corticosteroids for symptomatic relief of pruritus
- For patients with severe interstitial nephritis or interstitial pneumonia, systemic corticosteroids should be given.
- Prednisone 0.5 to 2 mg/kg per day is given until clinical improvement and normalization of laboratory parameters are obtained and then tapered over the ensuing 8 to 12 weeks. However, there is lack of consensus regarding steroid choice, dose, duration and route of administration

PREVENTION

- Educate patients about the need for a strict avoidance of the offending drug as well as cross-reacting drugs.
- Avoidance of the causative drug should also be recommended to family members of patients with DRESS because of suspicion of genetic factors.

ERYTHEMA MULTIFORME

BRIEF DESCRIPTION:

- An acute, immune-mediated condition characterized by the appearance of distinctive target-like lesions on the skin.Which is triggered by infection or drug.The most common infection associated with erythema multiforme is herpes simplex virus.
- Erythema multiforme is classified into EM minor and EM major. EM minor is characterized by localized skin lesion without mucosal involvement whereas EM major is characterized by wide spread epidermal detachment and one or more mucosal involvement.

CLINICAL FEATURES

Symptoms

- Cutaneous lesions are usually asymptomatic characterized by the appearance of distinctive target-like lesions on the skin

- Some patients experience itching and burning
- Prodromal symptoms are uncommon

Signs

- Target lesions with three concentric zones of color change: a central, dusky or blistered area, a dark red inflammatory zone surrounded by a pale ring of edema, and a peripheral, erythematous halo
- Frequently begin on the extensor acral extremities and may spread centripetally to other areas
- Painful erythematous patches, erosions, or bullae

INVESTIGATIONS AND DIAGNOSIS

- Diagnosis is clinical

TREATMENT

Goals of treatment

- Symptomatic management
- Identify cause

Pharmacologic

- Topical corticosteroids and oral antihistamines in case of EM minor.
- Anesthetic mouthwash
- For patients with EM major give oral Acyclovir
- Give Acyclovir for patients with HSV-induced recurrent EM and recurrent EM without an identifiable cause

Nonpharmacologic

- Withdraw if there is offending drug
- Wound care for extensive lesions
- Mouth and eye care for mucosal involvement

PREVENTION

- Continuous systemic antiviral therapy for patients with HSV associated or un identified cause

URTICARIA AND ANGIOEDEMA

BRIEF DESCRIPTION

- Urticaria is characterized by an intensely pruritic, circumscribed, raised, and erythematous eruption with central pallor.
- Angioedema is swelling of the deeper dermis and subcutaneous tissues that may coexist with Urticaria in as many as 50 percent of cases.
- In some cases, cutaneous Urticaria/angioedema is associated with systemic anaphylaxis.

CAUSES OF URTICARIA

- Acute urticarial are caused by food allergen, drug allergy, insect bites or infection.
- Chronic and recurrent urticarial are caused by environmental exposure to cold or hot weather, sun light exposure, exercise, pressure, emotional stress and chronic medical conditions such as diabetes mellitus, thyroid disorders, chronic renal insufficiency and biliary cirrhosis.

URTICARIA IS CLASSIFIED INTO ACUTE AND CHRONIC.

- Acute urticarial is considered when the onset is less than 6 weeks duration and chronic when it is more than 6 weeks duration.

CLINICAL FEATURES:

Symptoms

- Pruritus, burning of palms/ soles, auditory canal.
- With airway edema, difficulty breathing.
- Constitutional symptoms may be there.

Signs

- Urticaria: Large wheals that appear and resolve within a few hours, spontaneously or with therapy.
- Angioedema: Extensive tissue swelling with involvement of deep dermal and subcutaneous tissues.
- Often pronounced on face with skin colored enlargement of portion of face (eyelids, lips) or mucous membranes

INVESTIGATIONS AND DIAGNOSIS

- CBC
- Stool exam
- Skin prick testing
- Diagnosis is clinical

TREATMENT

Goals of treatment

- Provide immediate relief
- Prevent complications such as shock or asphyxiation

Nonpharmacologic

- Identification and removal of the offending trigger.

Pharmacologic

- Antihistamines: H 1 blockers or H 2 blockers or combination.
- Systemic Glucocorticoids:
- Intravenous Hydrocortisone or methylprednisolone for severe symptoms.
- Oral Prednisone, 70 mg, tapering by 10 or 5 mg daily over 1–2 weeks, is usually adequate.

PREVENTION

- The patient should carry information listing drug sensitivities (wallet card, bracelet).

REFERRAL:

- Chronic and recurrent urticarial cases should be refereed to dermatology center.

18.20 ECZEMA

ATOPIC DERMATITIS (AD)

- AD is a chronically relapsing, highly pruritic inflammatory skin disease which usually stats to occur during early infancy and childhood, the condition stats to go away after the age of 5 years but it may flare up and persists into puberty and sometimes adulthood.
- AD may be exacerbated by social, environmental, and biologic factors and has association to the other atopic diseases (allergic rhinitis, bronchial asthma and allergic sinusitis).

CLINICAL FEATURES

Infant

- usually begins as erythema and scaling of the cheeks.
- Lesions are symmetric and over cheeks, forehead, scalp, trunk and the extensor surfaces. Lesion may be papular or exudative.

Children:

- lesions are apt to be less exudative.
- The classic locations are the antecubital and popliteal fossae;
  - Flexor wrists, ankles, eyelids, face, and around the neck.
  - Lesions are often lichenified, indurated plaques.

Adolescents & Adults:

- Localized erythematous, scaly, papular, exudative, or lichenified plaques.
- In **adolescents**, the eruption often involves the classic-antecubital and

popliteal fossae;

- o Front and sides of the neck,
- o forehead, and area around the eyes.

- **In older adults,** the distribution is generally less characteristic, and chronic hand eczema may predominate. **S**imilar lesion with flexural distribution.

Diagnostic features of atopic dermatitis as defined by Hanifin and Rajka

MAJOR FEATURES (3 OF 4 PRESENT)

- Pruritus
- typical morphology and distribution of skin lesions
- chronic or chronically relapsing dermatitis
- personal or family history of atopy

MINOR FEATURES (3 OF 23 PRESENT)

1. Xerosis
2. Ichthyosis/palmar hyperlinearity/keratosis pilaris
3. Immediate (type I) skin test reactivity
4. Elevated serum IgE
5. Early age of onset
6. Tendency towards cutaneous infections/impaired cell-mediated immunity
7. Tendency towards non-specific hand or foot dermatitis
8. Nipple eczema
9. Cheilitis
10. Recurrent conjunctivitis
11. Dennie-Morgan infraorbital fold

12. Keratoconus
13. Anterior sub capsular cataracts
14. Orbital darkening
15. Facial pallor/erythema
16. Pityriasis alba amoebiasis anterior neck folds
17. Itch when sweating
18. Intolerance to wool and lipid solvents
19. Perifollicular accentuation
20. Food intolerance
21. Course influenced by environmental/emotional factors
22. White dermographism/delayed blanch

INVESTIGATION

- Clinical
- Serum IgE level in increased in most patients

TREATMENT

Goal of treatment

- Alleviate the pruritus, and prevent scratching.
- Decrease triggering factors
- Suppress inflammation
- Lubricate the skin
- Manage complications such as infection

Non pharmacologic

- do not use harsh soap and Atopic patients should bathe with cold or luke warm using mild soaps.

- Patient should dry quickly and immediately (within 3 minutes) and lubricate the skin.
- Avoid frequent washing

EMOLLIENTS:

- **Vaseline cream** OR **Liquid paraffin** applied liberally all over the body

PHARMACOLOGIC

First line

- Topical corticosteroids are the standard of care compared with other treatments:
- Eczematous lesions should be treated by mid-high strength topical steroids for up to 2 weeks except on the face, neck, breast, axillary, groin and perianal areas.
- For the face, neck, axilla and other soft areas of the body low-to-mild strength medications are preferred. Patients should apply the ointment after bathing.
- The use of long-term intermittent application of corticosteroids appears helpful and safe.
- N.B. Systemic steroids are preferably avoided.

PLUS

- **Cloxacillin** if a superimposed bacterial infection is suspected.

Antihistamines

- **Diphenhydramine**, 25-50mg P.O., QD or
- **Chlorpheniramine,** 4-6mg P.O., QD

CONTACT DERMATITIS

- The skin is the body's primary defense against environmental insults, it is frequently exposed to various noxious agents which can provoke a reaction known as contact dermatitis.

ALLERGIC CONTACT DERMATITIS (ACD)

- Allergic Contact Dermatitis is an inflammatory response of the skin to an antigen that can cause discomfort or embarrassment. It is due to delayed hypersensitivity reaction to exogenous allergens.
- Allergic contact Dermatitis can be classified as acute, subacute and chronic

CLINICAL FEATURES

- Acute contact dermatitis manifests by erythematous, indurated plaque or with fluid filled vesicles or bullae on an edematous skin
- Subacute contact dermatitis is characterized by less edema and formation of papules, excoriations and scaling
- Chronic eczema is characterized by scaling, skin fissuring and lichenfication.

IRRITANT CONTACT DERMATITIS (ICD)

- ICD is a non-immunologic inflammation of the skin caused by contact with physical or chemical agents. It manifests with edema and scaling and is non-specific response to the skin by irritants and direct chemical (cytotoxic) damage to the skin (e.g. corrosive agents which cause chemical burn). The hands are the most important sites of ICD.

CLINICAL FEATURES

- Macular erythema, hyperkeratosis or fissuring
- Glazed, parched or scalded appearance of the epidermis
- Healing process on withdrawal

Table 18. 1: Clinical features of Irritant Contact Dermatitis and Allergic contact dermatitis

	ICD	ACD
Symptom	Stinging, smarting, itching	Itching, pain
Lesions; Acute	Erythema, vesicle, erosion, crust, scaling	Erythema, **papules** vesicle, erosion, crust, scaling
Lesions; Chronic	Papules, plaques, fissures, scaling, crusts	Papules, plaques, fissures, scaling, crusts
Margination, site & evolution	Sharp, strictly confined to site of exposure	Spreading in the periphery; usually tiny papules; may become generalized
Causative agent	Dependent on concentration of agent and state of skin barrier	Relatively independent of amount agents and state of skin barrier
Incidence	May occur in practically everyone	Occurs only in the sensitized

IRRITANT VERSUS ALLERGIC CONTACT DERMATITIS

Investigations

- KOH mount and culture to rule out fungal infection.
- Patch testing can be done to rule out ACD.
- Skin biopsy can help exclude other disorders such as fungal infection, psoriasis, cutaneous T-cell lymphoma

TREATMENT

Goals of treatment

- Improve the quality of life by reducing symptoms.

Non pharmacologic

- Self-care at home and removal of the offending agent
- Avoid scratching and Lukewarm water baths (antipruritic)

Emollients:

- Vaseline cream OR Liquid paraffin applied liberally to affected area

For acute lesions

- Topical soaks with cool tap water plus saline (TSP/Pint)
- Oat meal bath

Pharmacologic

Topical steroids:

First line

- **Triamcinolone acetonide**, thin films applied BID initially, reduce to once daily as lesions remit.

Alternative

- **Hydrocortisone**, thin films applied on face, axillae, breasts, groins and perianal area twice daily initially, reduce as the lesion's remits. Or
- **Mometasone**, thin films applied QD

Systemic

- **Systemic steroids** (for severe, recalcitrant and generalized cases)
- **Prednisone**,0.5mg/kg P.O. QD for 1-2 weeks.

SEBORRHOEIC DERMATITIS

BRIEF DESCRIPTION

- Seborrhoeic dermatitis is a very common inflammatory scaling disease confined to areas of high sebum production and body folds.
- It affects the scalp, face and occasionally other areas with high density of oil glands such as the axilla, upper chest and anogenital areas.

- It is linked to high sebum production, Immunosuppression, Malassezia yeast.
- It ranges from mild dandruff to exfoliative erythroderma which usually is associated with immunosuppression.

CLINICAL FEATURES

Infants:

- Begins about one week after birth and may persist for several months.
- It presents with greasy scales adherent to the vertex (cradle cap).
- Lesions can also involve body folds with cracking, erythema and greasy scale.

Adults:

- Mild scalp lesion but extensive scaling and thick adherent crusts can also occur
- Lesion may extend from the scalp to involve the forehead, retroarticular area central upper chest and the intertriginous areas.

Investigation

- Diagnosis is Clinical

TREATMENT

Goal of treatment

- Reduction of erythema and itching
- Control of secondary infection

Non pharmacologic

- Bathing and application of emollient use
- Wash hair with shampoos containing 2% ketoconazole or selenium sulphide 2.5% shampoo.

PHARMACOLOGIC

TOPICAL

- 4% salicylic acid in olive oil or water-soluble base for removal of crust
- Apply Topical corticosteroid solutions, lotions or ointments such as
- 1 % hydrocortisone,
- Fluocinolone acetonide,0.01 %in oil is helpful
- 2 % ketoconazole cream applied one or two times daily

SYSTEMIC

- Systemic antifungals and occasionally systemic corticosteroids are used in few cases

18.21 PSORIASIS

BRIEF DESCRIPTION

- Psoriasis is a common, chronic, and recurrent inflammatory disease of the skin that has significant impact on quality of life.
- It is characterized by circumscribed, erythematous, dry scaling plaques of varying sizes often with predilection to certain parts of the body.
- Psoriasis is an immune mediated disease and is usually a lifelong disease.
- Physical trauma, stress, alcohol, stress and infections including HIV, are some of the factors that trigger and exacerbate psoriasis.

CLINICAL FEATURES

- It can present in many different patterns and can range from mild lesions to severe generalized lesions affecting every part of the skin.
- Skin lesion characterized by circumscribed plaques with erythematous base and, silvery-white dry scaling of varying sizes often with predilection to certain parts of the body

- The most common sites of involvement are the scalp, elbows and knees, followed by the nails, hands, feet and trunk (including the intergluteal fold).

INVESTIGATIONS

- Clinical
- Histopathologic Examination

TREATMENT

Goals of treatment

- Relieve symptoms

Non pharmacologic

- Explain regarding precipitating factors, chronicity and nature of the disease
- Counseling the patient never to rub or scratch lesions (to minimize Koebner's phenomenon).
- Phototherapy or photochemotherapy

PHARMACOLOGIC FOR LOCAL PLAQUES

General Measures

- Liberal use of moisturizers like urea, petrolatum and liquid paraffin between treatments.
- It helps to keep skin soft and limit pruritus and irritation,
- Removal of excessive scale by soaking in water or by using salicylic acid, 5–10% in **Vaseline** base applied twice daily

Topical

First line

- **Betamethasone dipropionate**, thin film applied twice daily for short period of time are effective. For lesions of the face, neck, flexural areas and genitalia mild potency steroids are preferred.
- **Dithranol**, started using low concentrations (0.05 to 0.1%) incorporated

in petrolatum or zinc paste and given once daily. To prevent auto oxidation, salicylic acid (1 to 2%) can be added. Short contact therapy (minute therapy for 10-30 minutes). The concentration is increased weekly starting from 1% up to about 5% until the lesions resolve, then it can be tapered and discontinued gradually.

- **Calcipotriene**, thin films applied twice daily at the area of plaques. Not more than 100gms per week should be used. Exposure to sunlight facilitates remission. Salicylic acid should not be used in combination with **calcipotriol** due to the possible inactivation of this compound by the former.
- **Retinoid tazarotene jell or cream** is applied once or twice daily.
- Coal tar reduced scaling itching and inflammation of the skin lesion but it stains the cloth.
- **Goeckerman** therapy: combine coal tar treatment with sun light exposure

SYSTEMIC

- For patients who failed to respond to topical therapy, refer the patient to be seen by dermatologist.

18.22 VITILIGO

BRIEF DESCRIPTION

- Vitiligo is a common acquired, progressive loss of pigmentation.
- The exact cause is not known. melanocytes of the basal layer are destroyed because of autoimmune or auto inflammatory destruction of melanocytes or intrinsic abnormality within melanocytes themselves.

CLINICAL FEATURES

- Asymptomatic, chalk-white, non-scaling macules or patches with well-defined borders.
- Extensor bony surfaces and the periorofacial areas are commonly affected

areas.

Investigation

- Diagnosis is clinical
- Lab investigation like TSH and FBS is indicated, as Vitiligo can be associated with endocrine disorders such as hypothyroidism and diabetes mellitus.

TREATMENT

Goal of treatment

- To promote re-pigmentation

Non pharmacologic

- Explain about the nature and unpredictability of the disease
- Counseling and psychological support of patients

Pharmacologic

Topical

- Potent or very potent corticosteroids applied twice daily for up to three months.
- There should be one-week gap for every three weeks application.

SYSTEMIC

- Oral glucocorticoids such as low dose prednisolone can be effective in patients with progressive disease which is difficult to teat with topical steroid and photochemotherapy.

CHAPTER 19:

EYE DISEASES

19.1 MAJOR BLINDING EYE DISEASES

ATARACT

BRIEF DESCRIPTION:

- It is any congenital or acquired opacity in the lens and/or lens capsule
- It is the leading causes of blindness in Ethiopia and worldwide
- Age related cataract is the most common; others are due to trauma, uveitis, systemic disease (like diabetes mellitus), steroid uses and congenital
- Cataract surgery is the most frequently performed surgical procedure
- Classified on the basis of etiology, maturity, morphology

CLINICAL FEATURES:

Symptoms

- Gradual reduction of vision, glare in sunshine or with street/car lights
- Altered colours - white objects appear yellowish, monocular double vision

Signs

- Reduced visual acuity up to the level of light perception
- Lens opacity

Investigations and diagnosis: Clinical

TREATMENT

Goal of treatment

- To restore the vision

Non-pharmacological treatment

- Surgical removal of the cataract

Pharmacological treatment

- None

Referral: Refer all cases to ophthalmologist or cataract surgeon for surgical management

GLAUCOMA

BRIEF DESCRIPTION:

- It is a group of diseases characterized by progressive optic neuropathy and visual field loss
- It is a major blinding disease worldwide and the leading cause of irreversible blindness
- Classified based of etiology, age of onset, mechanism, chronicity, and more
- Usually bilateral, but may be unilateral or asymmetrical (usually secondary)
- Primary risk factor is elevated IOP (> 21 mm Hg), "normal IOP" doesn't rule out glaucoma
- Others risks are advanced age, positive family history, race, refractive error, eye surgery or injury, steroid use, inflammation, refractive error.
- Primary open angle and Pseudoexfoliative glaucoma are the commonest types in Ethiopia

ACUTE GLAUCOMA

(See subtopic under red eye)

Chronic Glaucoma

Clinical features:

Symptoms

- Mostly asymptomatic ("sight thief")

- History of gradual loss of vision in the affected eye or loss of visual field

Signs

- Cupping of optic disc on fundoscopy and /or elevated IOP
- RAPD (useful to detect an eye with advanced glaucoma)
- Digital palpation to compare both eyes

Investigations and diagnosis:

- Tonometry measures intraocular pressure (IOP)
- Visual field test (confrontation, FDT, standard perimetry)
- Ophthalmoscopy fundus examination

TREATMENT

Goal

- Early detection, control intra-ocular pressure and preserve vision
- Maintain the IOP to the safe level that does not cause damage
- Halt progressive optic nerve head damage and visual field loss
- Decrease the medication side effects

Non-pharmacological treatment

- Surgery – Trabeculectomy, Tube-shunt implant
- Laser treatment

Pharmacological treatment

Chronic open angle glaucoma

Beta adrenergic antagonist

- Timolol 0.25% or 0.5% eye drops, instill 1 drop BID

OR

- Betaxolol 0.5% eye drops, instill 1 drop BID

PROSTAGLANDIN ANALOGUES:

- Latanoprost 0.005% eye drops, instill 1 drop daily if target IOP not reached
- NB. Currently prostaglandin analogue eye drops are the first line, if available
- Also, can be used alone in cases of intolerance and contraindications to betablockers
- **Alternative**: Travoprost 0.004%,

ADRENERGIC AGONISTS

- Brimonidine 2% eye drops, instill 1 drop BID
- Apraclonidine eye drop, instill BID or TID

NB. Use as second line if patient has allergic reaction to prostaglandin analogue, in place of prostaglandin analogue and/or in combination with ß-blocker. Avoid use in children less than 2 years.

Combination drugs can be used if the patient has poor response. Combinations should be from different therapeutic classes.

PARA SYMPATHOMIMETIC:

- Pilocarpine, 2 and 4%, eye drops, instill 1 drop QID, drug of choice in pigmentary glaucoma
- NB. Avoid use in young patient (except in pigmentary Galucoma), uveitic glaucoma, and primary open angle glaucoma (POAG) with high myopia

CARBONIC ANHYDRASE INHIBITORS:

- Acetazolamide 125 to 250mg, BID to QID or Methazolamide 50 to 100mg, BID to TID
- Dorzolamide 2% eye drop 1 drop BID or TID or Brinzolamide 1% eye drop, 1 drop BID to TID
- NB: The oral preparations only used in cases of very high IOP used for short period, due to side effects

Referral: Refer all cases of glaucoma and/or glaucoma suspect to an ophthalmologist

TRACHOMA

BRIEF DESCRIPTION:

- Trachoma is a chronic cicatrizing keratoconjunctivitis
- Caused by Chlamydia trachomatis, serotype A, B and C more common
- Primarily affects the superior and inferior tarsal conjunctiva and cornea, also eyelids
- Trachoma is related to poor hygiene, and is a disease of poverty
- Important and major cause of avoidable/preventable blindness in the world

CLINICAL FEATURES:

Symptoms

- Nonspecific - foreign body sensation, redness, tearing and mucopurulent discharge
- Spot in the cornea or reduction in vision (as a sequel of previous trachoma attack)

Signs

- Active trachoma – conjunctival follicles and papilla
- Conjunctival scarring, entropion of the eyelid and trichiasis
- Corneal neovascularization and opacity, Herbert's pit at the limbus

Investigations and diagnosis: Clinical

World Health Organization (WHO) Classification

Active trachoma with follicle (TF)

- At least 5 follicles in upper tarsus, also some papilla
- Palpebral conjunctival blood vessels ae clearly visible
- Represent active moderate infection, needs treatment

ACTIVE TRACHOMA WITH INTENSE INFLAMMATION (TI)

- Many follicles and/or papillae
- Palpebral conjunctival blood vessels are completely or almost obscured
- Represent active severe infection, needs urgent treatment

TRACHOMATOUS SCARRING (TS)

- White scars are present on upper tarsus
- Represent prior/old infection, now inactive

TRACHOMATOUS TRICHIASIS (TT)

- At least one eyelash rubbing against the cornea or prior epilation
- Likely to develop progressive corneal scarring, needs surgical treatment

CORNEAL SCARRING (CO)

- Corneal opacity affecting central cornea
- Visual loss from previous trachoma, now inactive

Treatment and prevention

World Health Organization (WHO) advocates SAFE strategy

S = Surgery for complications (TT & CO)

A = Antibiotics for active (inflammatory) trachoma (TT & TI)

F = Face washing, particularly in children

E = Environmental improvement including provision of clean water

Goal of treatment

- Early Identification and treatment
- Prevent complications

Non-pharmacological treatment

- Surgical correction of entropion/trichiasis (TT)

- Penetrating Keratoplasty if indicated (CO)

PHARMACOLOGICAL TREATMENT

I. TRACHOMATOUS INFLAMMATION – FOLLICULAR (TF)

Topical treatment (effective, cheaper, minimal systemic side effect)

- Tetracycline 1% ointment single strip apply BID to QID for 6 weeks OR
- Erythromycin 0.5% ointment single strip apply BID for 6 weeks

II. TRACHOMATOUS INFLAMMATION -INTENSE (TI)

- Topical (see above under TF)
- Systemic treatment
- Azithromycin 1gm PO stat for adult and 20 mg/kg stat in children (“Magic bullet”)

FURTHER READING

1. World Health Organization. Trachoma control: A guide for Programme managers. WHO 2006

19.2 RED EYES

BRIEF DESCRIPTION:

- Many causes of red eye are benign, but the initial goal in evaluation should be to identify conditions that require referral (emergent) to an ophthalmologist
- Conjunctivitis is the most common cause of red eye, but always attempt to exclude other more serious causes

Table 19.1 Differential diagnosis of Red eyes

Painful red eye	Only mild discomfort
Bacterial Keratitis	Allergic conjunctivitis
Anterior uveitis	Bacterial conjunctivitis
Episcleritis/scleritis	
Acute angle closure glaucoma	
Ocular trauma	
Herpetic keratitis	
Endophthalmitis	
Ocular chemical burn	

HISTORY

- Trauma- when, where, with what object, wearing of protective eyeglass during incident
- Chemical contact – type of solution, amount, concentration, immediate action
- Prior known ocular diseases e.g. glaucoma, herpetic keratitis or ocular surgery
- Current medication use (topical and systemic), if there is known drug allergies
- Traditional medicine application, inquire about vegetative injury (risk of fungal infection)
- Uses of contact lens
- Systemic diseases e.g.,TB, syphilis, rheumatoid arthritis, retroviral infection

OCULAR EXAMINATION

- Always check vision (medico legal, baseline for follow up)
- Watch out for not to transmit infection while measuring EYE pressure
- Eye movement (restrictive and/or paralytic cranial nerves palsies)

- Pupillary size, and reactivity (optic nerve status)
- Perform fundoscopy examination with direct ophthalmoscope (posterior segment status)
- Thorough anterior segment and orbital evaluation

NB. Always rule out sight/ light threatening causes, before considering red eye as conjunctivitis!

RED EYE WITH SIGNIFICANT/SEVERE PAIN

CORNEAL ULCER (BACTERIAL KERATITIS)

BRIEF DESCRIPTION:

- Destruction of corneal tissue due to inflammation from infectious organisms
- Risk includes trauma, dry eye, lid abnormalities, immunosuppression, contact lens wear
- Usually due to ***staph aureus, staph epidermidis, P. aeruginosa, M. catarrhalis***. Organisms that penetrate intact cornea includes: ***N. gonorrhea, N. meningitides, C. diphtheriae and H. influenzae***. It is important to remember that infections may be polymicrobial.
- It is important to note that the causative organism cannot be defined reliably from the morphological appearance of the ulcer

CLINICAL FEATURES:

Symptoms

- Pain, discharge, photophobia, red eye, decreased vision, white spots on cornea

Signs

- Normal or decreased visual acuity

- Conjunctival injections, corneal edema, reduced corneal sensation
- Corneal infiltrate with overlying epithelial defect

Investigations and diagnosis

- Corneal staining with Fluorescein stain, tonometry (IOP)
- Corneal ulcer scrape for microbiology in cases of large epithelial defect

TREATMENT

Goal of treatment

- Treat the infection and prevent corneal scarring

Non-pharmacological treatment

- Discontinuation of contact lens wear is mandatory
- Plastic eye shield should be worn if significant thinning (or perforation) is present

PHARMACOLOGICAL TREATMENT

I. Small infiltrates (< 2 mm): broad-spectrum topical antibiotic. Refer if there is no response within 48 hours.

II. Large ulcer: administering broad spectrum agents active for gram positive and gram-negative pathogens topical antibiotics (fortified antibiotic possible, see annex about antibiotic fortification) and refer.

Referral. Early referral to ophthalmological treatment center for all cases of corneal ulcer

CHEMICAL BURN

BRIEF DESCRIPTION:

- Chemicals include alkaline, acids, solvents, detergents, and irritants
- Alkali causes most severe injury than acids and may cause perforation
- The majority are accidental, but a few are due to assault

CLINICAL FEATURES

Symptoms

- Pain, red eye, foreign body sensation, photophobia, tearing

Signs

- Conjunctival chemosis, hyperemia, and/or haemorrhage
- First, second or third degree burn of the periorbital skin
- Danger signs
- ○ Corneal epithelial defects
- ○ Pronounced chemosis and perilimbal blanching
- ○ Corneal edema and opacification

Investigations and diagnosis

- Corneal staining with fluorescein or Rose Bengal stains

TREATMENT

Goal of treatment

- Prevent corneal dryness, ulceration and infection
- Avoid corneal opacity and blindness

Non-pharmacological treatment (emergent action)

- Copious irrigation of the eyes, preferably with NS or RL solution, for at least 30 minutes
- However, if tap water is the only available liquid, it should be used
- Pull down the lower eyelid and even the upper eyelid, if possible, to irrigate the fornices
- Measure pH after irrigation, continue irrigation until pH is neutralized

PHARMACOLOGICAL TREATMENT

- Analgesia to control pain, prophylactic topical antibiotic drops

- Apply available antibiotic ointment with pressure patch for 24 hours
- **Referral**. Early referral to an ophthalmologist immediately if the injury is severe. In mild cases, evaluate after 24 hours and refer the patient if the vision is still compromised.

ACUTE CLOSED ANGLE GLAUCOMA

BRIEF DESCRIPTION:

- Acute attack usually occurs in one eye
- Without treatment, progress to permanent damage and blindness, especially in old age
- The affected eye feels harder compared to the other eye when measured with finger palpation

CLINICAL FEATURES:

Symptoms

- Sudden onset of severe eye pain and redness, photophobia
- Associated with nausea, vomiting and hemi-cranial headache
- Markedly decreased vision, blurring ('smoke-filled room') and haloes ('rainbow around lights')

Signs

- Hazy or edematous cornea, mid-dilated non-reactive pupil
- Shallow anterior chamber, usually severely elevated IOP (50 to 80 mm Hg)

Investigations and diagnosis

- Tonometry measure of intraocular pressure (IOP); alternatively, digital palpation to compare with the other eye.
- Ophthalmoscopy fundus examination

TREATMENT

Goal of treatment

- Institute initial therapy and then refer to hospital with ophthalmology unit (if there is no an ophthalmologist)
- Try to achieve immediate reduction in IOP

Non-pharmacological treatment

- Supine position to encourage the lens to shift posteriorly under the influence of gravity
- Laser peripheral iridectomy, if the attack not broken medically

Pharmacological treatment

- Acetazolamide 500mg PO (IV if IOP > 50 mm Hg) stat, followed by 250mg 6 hourly PLUS
- Timolol 0.5% eye drops, instill 1 drop every 15 minutes 2x, then BID

N.B. Where those above measures fail, for short-term use only:

- Mannitol 1 to 2 g/kg as a 20% solution IV over 30 to 60 minutes OR

Glycerol 1 g/kg of 50% solution PO stat immediately

HERPES SIMPLEX (HERPETIC) KERATITIS

Brief description:

- Caused by herpes simplex virus (HSV 1, rarely HSV2), it can be primary or recurrent
- May present similarly to viral conjunctivitis, except it is usually unilateral
- It is the most common infectious cause of corneal blindness in developed world

Clinical features:

Symptoms

- Pain, photophobia, tearing, redness, blurry vision

Signs

- Look for classic dendritic ulcer on the cornea, reduced corneal sensation

INVESTIGATIONS AND DIAGNOSIS:

- Corneal staining with fluorescein stain

TREATMENT

Goal of treatment

- Treat the infection
- Prevent recurrence

Non-pharmacological treatment

- Avoid steroid use, which exacerbate the infection in epithelial keratitis
- Debridement may be used for resistant cases
- Conjunctival flap for large indolent ulcer and corneal perforation
- Penetrating keratoplasty if indicated

Pharmacological treatment

Initial therapy

- Acyclovir 3% ointment 5 times per day OR
- Acyclovir 400 mg 5 times per day 10 to 14 days (indicated in most immunodeficient patients, in children and patients with marked ocular surface disease)

MAINTENANCE THERAPY

- Acyclovir 400 mg po BID, up to 1 to 2 years

Referral. Early referral to eye care in all cases of Herpetic keratitis is recommended if there is no an ophthalmologist. Initiating acyclovir may be important before referral, however, steroid should be avoided.

IRITIS/IRIDOCYCLITIS (ANTERIOR UVEITIS)

BRIEF DESCRIPTION:

- It is an inflammation of anterior uveal tract i.e. the iris and the anterior ciliary body

- Predominantly HLA-B27-related and idiopathic forms make up the largest proportion
- Systemic diseases associated are TB, syphilis, sarcoidosis, juvenile rheumatoid arthritis

CLINICAL FEATURES:

Symptoms

- Pain, red eye, photophobia, blurring of vision, watery discharge

Signs

- Cell and flare, Keratic precipitates (KP), hypopyon
- Iris nodules, atrophy, heterochromia and synechiae
- Ciliary flash, Intraocular pressure (IOP) can high or low

Investigations and diagnosis

- Systemic work up - CBC, VDRL, RF, serology for HIV, chest X-ray

TREATMENT

Goal of treatment

- To relieve the inflammation and/or prevent flare up
- To prevent and/or treat secondary glaucoma

Non-pharmacological treatment

- Watch the intraocular pressure (IOP) carefully while using topical steroids
- Follow daily to every week in acute phase, then every 1 to 6 months

Pharmacological treatment

- Cycloplegic agent: atropine 1%, homatropine 5% or tropicamide eye drops BID to QID
- Topical steroids: dexamethasone eye drops every 1 to 6 hours, depends on severity

- Treat secondary glaucoma (Pilocarpine and prostaglandins are contraindicated!)
- Treat the underlying systemic diseases

Referral: refer all cases of suspected anterior uveitis to higher eye care center

OCULAR TRAUMA

BRIEF DESCRIPTION:

- Eye injuries generally classified as penetrating and blunt
- Occupational ocular injuries and injuries during a fight are common
- In severe cases neurosurgery, ENT and/or maxillofacial surgery are needed

CLINICAL FEATURES:

Symptoms

- Painful red eye, swelling, bleeding, foreign body sensation

Signs

- Always first check visual acuity and document appropriately
- Gross facial asymmetry due to orbital bones fractures or soft tissue swelling
- Subconjunctival hemorrhage, proptosis in retrobulbar hemorrhage
- Corneal and/or conjunctival abrasion, foreign body, tear

Investigations and diagnosis

- Skull x-ray and/or Orbital CT scan, safe for fracture and metallic foreign body

TREATMENT

Goal of treatment

- To save the sight and prevent posttraumatic infections

- To maintain the globe If the visual acuity is no light perception

Non-pharmacological treatment

- Avoid any instillation of eye drops in penetrating ocular injuries
- Early referral to tertiary eye care center

Pharmacological treatment

- For penetrating eye injury: Systemic antibiotics, TAT
- Analgesia for pain control

REFERRAL TO EYE CARE CENTER

- All patients with trauma involving eyelid margin
- All cases with ocular or orbital foreign body
- All cases with orbital and cranial nerve injuries
- All patient with open globe (perforated eyeball)
- Reduction of vision after sustained trauma with non-evident explanation

ENDOPHTHALMITIS

BRIEF DESCRIPTION:

- Intraocular infection, can be acute(symptomatic), subacute and chronic (asymptomatic)
- It can be postoperative (most common), posttraumatic and rarely endogenous
- Prognosis depends on the etiology, duration and organism, usually poor in posttraumatic

CLINICAL FEATURES:

Symptoms

- Pain, red eye, photophobia, decreased vision

Signs

- Decreased visual acuity, poor red reflex
- Lid edema, Conjunctival injections and chemosis, proptosis
- Corneal edema, anterior chamber cell and flare, hypopyon, Keratic precipitates

INVESTIGATIONS AND DIAGNOSIS

- B scan if fundus is not visualized

TREATMENT

Goal of treatment

- Treat the infection
- Prevent sight- and/or life-threatening complications

Non-pharmacological treatment

- Daily follow up in acute phase, then according to the treatment response

Pharmacological treatment

- Intravitreal antibiotics
- Broad spectrum fortified topical antibiotic (fortified antibiotic possible, see annex about antibiotic fortification)
- Topical steroids
- Systemic intravenous antibiotics for marked inflammation, severe cases

Referral. Early referral to eye care center is recommended for all cases of suspected Endophthalmitis

RED EYE WITHOUT SIGNIFICANT PAIN

ALLERGIC CONJUNCTIVITIS

BRIEF DESCRIPTION:

- Atopy is a genetically determined predisposition to hypersensitivity reactions upon exposure to specific environmental antigens

- It is Type I, mediated by degranulation of mast cells in response to action of IgE
- There is evidence of an element of Type IV hypersensitivity in at least in some forms
- There are various forms of allergic conjunctivitis

ACUTE ALLERGIC CONJUNCTIVITIS

BRIEF DESCRIPTION:

- A common condition, an acute reaction to an environmental allergen (usually pollen)
- It is typically seen in younger children after playing outside in spring or summer

CLINICAL FEATURES:

Symptoms

- Conjunctival swelling, acute itching, watering

Signs

- Chemosis is the hallmark (frequently dramatic and worrying to the child and parents)

Investigation and diagnosis: Clinical

TREATMENT

Goal of treatment

- To relieve the symptom

Non-pharmacological treatment

- Cold compress (e.g. washing with refrigerated water, putting a clean refrigerated towel or ice pack)

PHARMACOLOGICAL TREATMENT

- Dexamethasone 0.1% BID to QID

HAY FEVER AND PERENNIAL ALLERGIC CONJUNCTIVITIS

BRIEF DESCRIPTION:

- Common subacute conditions, distinguished from each other
- Often other atopic conditions, such as allergic rhinitis and asthma

Hay fever	Seasonal	Perennial
Prevalence	• More common	• Less common
Allergens	• Tree & grass pollens	• Mites, dander, fungus
Exacerbation season	• Spring and summer	• Autumn
Severity	• Mild to severe	• Usually, mild

CLINICAL FEATURES:

Symptoms

- Intense itching is a hallmark symptom, attacks are usually short lived and episodic
- Eyelid swelling, mucoid eye discharge, associated with sneezing and nasal discharge

Signs

- Conjunctival hyperemia and chemosis, relatively mild papillary reaction, lid edema

Investigations and diagnosis

- Conjunctival scraping to look characteristics of eosinophils or their granules

TREATMENT

Goal of treatment

- Avoid exposure to allergen
- Alleviate the symptoms

Non-pharmacological treatment

- Identify and avoid the allergens
- Cold compresses

Pharmacological treatment (see under Atopic keratoconjunctivitis)

Topical

- Artificial tears for mild symptomatic
- Antihistamines for symptomatic exacerbation
- Mast cell stabilizer for long term use
- Combination

Systemic

- Oral antihistamines may be indicated for severe symptoms

VERNAL KERATOCONJUNCTIVITIS (VKC)

BRIEF DESCRIPTION:

- Recurrent bilateral disorder, IgE- and cell-mediated immune mechanisms play roles
- Primarily affects boys and onset is generally from about the age of 5 years onwards
- Frequently but not invariably have personal or family history of atopy
- Often occurs on a seasonal basis, with a peak incidence over late spring and summer, although there may be mild perennial symptoms
- There is remission by the late teens in 95% of cases, although many of the remainder develop atopic keratoconjunctivitis

CLINICAL FEATURES:

Symptoms

- Intense itching, lacrimation, photophobia

- Foreign body sensation, burning and thick mucoid discharge
- Increased blinking is common

Signs

- Conjunctival hyperemia and diffuse velvety papillary hypertrophy on superior tarsal plate in palpebral form, micro to giant papilla ("cobble stone" appearance)
- Different forms of keratoplasty are more frequent in palpebral disease
- Horner -Trantas dot in limbal form (also may find in atopic keratoconjunctivitis)
- Pseudogerontoxon i.e. perilimbal band of superficial scarring can develop in recurrent limbal disease, resembling arcus senilis

Investigations and diagnosis: Clinical

TREATMENT

Goal of treatment

- Relieve symptomatic surface disease
- Prevent complications

Non-pharmacological treatment

- Climatotherapy such as the use of air-conditioning or relocation to cooler environment
- Ice packs and frequent face washing with cold water gives temporary relief
- Avoid eye rubbing, which is partly responsible cause for corneal ectasia

Pharmacological treatment

- Mild: Topical antihistamine +/- NSAIDS
- Moderate: topical mast cell stabilizer +/- NSAIDS
- Severe: Steroid +/- topical antihistamine +/- NSAIDs +/- mast cell stabilizer
- NB. Corticosteroids should be reserved for exacerbations with moderate

to severe discomfort and/or decreased visual acuity and should be discontinued between attacks. The patient and family must be thoroughly informed about the potential risk of chronic steroid therapy

Referral: In severe and complicated cases refer to an ophthalmologist

ATOPIC KERATOCONJUNCTIVITIS (AKC)

BRIEF DESCRIPTION:

- A rare bilateral disease that typically develops in adulthood (peak incidence 30 to 50 years) following a long history of atopic dermatitis (eczema)
- Asthma is also extremely common in these patients. About 5% have suffered from childhood VKC
- Eosinophils tend to be less common in conjunctival scrapings than with VKC
- Associated chronic staphylococcal blepharitis and madarosis are common

CLINICAL FEATURES:

Symptoms

- Similar to those of VKC, but are frequently more severe and unremitting
- Discharge is generally more watery

Signs

- Eyelid erythema, dryness, scaling and thickening
- There may be keratinization of the lid margin.
- Hertoghe sign: absence of the lateral portion of the eyebrows
- Dennie–Morgan folds: lid skin folds caused by persistent rubbing

Investigations & diagnosis: Clinical

TREATMENT

Goal of treatment

- To alleviate the symptoms

- Treat associated blepharitis

Non-pharmacological treatment

- Allergen avoidance
- Cold compress
- Lid hygiene for associated blepharitis

PHARMACOLOGICAL TREATMENT

Topical:

- Vasoconstrictor: Tetrahydrozoline 0.05% or Oxymetazoline 0.025% or 0.05%, 1 drop TID to QID, not more than one week (due to rebound conjunctivitis)
- Vasoconstrictors- antihistamine combination: Naphazoline + Antazoline 0.025%+0.5% or Naphazoline + Phenylephrine 0.25% + 0.3%, 1 drop TID to QID
- Antihistamine: Levocabastine 0.05% or Olopatadine 0.1%, 1 drop TID to QID
- Mast cell stabilizer: Cromolyn Sodium 4% or Lodoxamide 0.1%, 1 drop TID to QID
- NSAIDs: Diclofenac 0.1% or Flurbiprofen 0.03% or Ketorolac 0.5% or Suprofen 0.5%, 1 drop TID to QID
- Artificial tears, 1 drop 3 to 5 times per day
- Steroid: Dexamethasone 0.1% or Prednisolone 0.25%, and 1% or Fluoromethalone 0.1%, 0.25%, every 2 to 4 hours per day depending on the severity and tapered every 5 to 7 days down to 1 drop every other day
- Steroid – antibiotics combination: Dexamethasone + Chloramphenicol 0.1% + 0.5% or Dexamethasone + Tobramycin 0.1% + 0.3%, 1 drop every 2 to 4-hour, taper as steroid

NB. Treatment should be based on the severity of patient symptoms, and consists of one or more the above medications. Mast cell stabilizer not effective against acute attack, due to slow onset of effect

Systemic: oral antihistamine may provide symptomatic relief in some patients

BACTERIAL CONJUNCTIVITIS

ACUTE BACTERIAL CONJUNCTIVITIS IN CHILDREN AND ADULT

BRIEF DESCRIPTION:

- A common and usually self-limiting condition caused by direct contact with infected secretions, about 60% resolve within 5 days without treatment.
- In children, the possibility of progression to systemic involvement should always be borne in mind
- The most common isolates are Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae and Moraxella catarrhalis
- Other rare isolates are Neisseria gonorrhea (sexually active individuals) & Neisseria meningitides (in children)

CLINICAL FEATURES:

Symptoms

- Acute onset of redness, grittiness, burning and discharge
- Involvement is usually bilateral although one eye may become affected 1–2 days before the other
- On waking, the eyelids are frequently stuck together and may be difficult to open

Signs

- Visual acuity is not usually affected
- Generalized conjunctival hyperemia and chemosis
- Muco-purulent eye discharge, gumming of eye lashes
- Palpable LNs in severe gonococcal & meningococcal infections

INVESTIGATIONS AND DIAGNOSIS:

- Conjunctival swab & scrapings for Gram's stain & culture and sensitivity for severe cases

TREATMENT

Goal of treatment

- Treat the infection
- Prevent re-infection, transmission and complications

Non-pharmacological treatment

- Frequent cleaning of the eyelids and warm compression

PHARMACOLOGICAL TREATMENT

Topical antibiotics

- Chloramphenicol, 0.5 % solution 1 drop every 4 to 6 hours or 1% ointment single strip apply BID to QID for 10 to 15 days OR
- Tetracycline 1% ointment, single strip apply BID to QID for one to two weeks OR
- Ciprofloxacin 0.3 % solution, 1 drop every 4 to 6 hours per day for one to two weeks OR
- Tobramycin 0.3% eye drop, 1 drop every 4 to 6 hours per day for one to two weeks

SYSTEMIC ANTIBIOTICS ARE REQUIRED IN CASES OF

- Gonococcal infections, ceftriaxone or quinolones
- H. influenzae in children, amoxicillin/clavulanate
- Meningococcal infections in children
- NB. Frequent topical instillation of antibiotic eye drops or ointments is useful (it speeds recovery, re-infection and transmission). Quinolones (such as ciprofloxacin eye drop should be reserved for refractory (resistant) cases to initial therapy.

Referral: In severe and complicated cases refer to an ophthalmologist

NEONATAL CONJUNCTIVITIS (OPHTHALMIA NEONATORUM)

Brief description:

- Conjunctival inflammation developing within the first month of life
- It is identified as a specific entity distinct from conjunctivitis in older infants because of its potentially serious nature (both ocular and systemic complications)
- Common etiologies C. Trachomatis and N Gonorrhea; other HSV 2, staphylococcus, chemical conjunctivitis (prophylaxis eye drops, silver nitrate) and congenital NLDO
- Gonococcal conjunctivitis is a serious infection and, if untreated, it progresses to corneal ulceration/perforation and endophthalmitis, leading to blindness.

CLINICAL FEATURES:

Symptoms

- Rapid progressive copious purulent conjunctival discharge

Timing of onset

- Chemical irritation: first few days
- Gonococcal: first week
- Staphylococci and other bacteria: end of the first week

○ Herpes simplex virus (HSV): 1–2 weeks

○ Chlamydia: 1–3 weeks

Signs

- Marked conjunctival hyperemia and chemosis

Investigations and diagnosis:

- Gram's stain and culture from discharge in moderate to severe cases

TREATMENT

Goal of treatment

- Treat the infection
- Prevent corneal perforation and blindness

Non-pharmacological treatment

- Saline irrigation to remove excessive discharge

PHARMACOLOGICAL TREATMENT

Mild conjunctivitis – Topical antibiotics

- Tetracycline 1% ointment, single strip apply BID to TID for 2 weeks OR
- Erythromycin 1% ointment, single strip apply BID to TID for 2 weeks OR
- Chloramphenicol, 0.5% eye drop 1 to 2 drops TID to QID or 1% ointment single strip apply BID to TID OR
- Gentamicin 0.3% solution, 1 to 2 drops 4-6 times daily for 10 to 15 days

NB. For chemical conjunctivitis, avoid the offending agent and use artificial tears if needed

Moderate to Severe – systemic antibiotics

Chlamydial infection

- Erythromycin po for 2 weeks

GONOCOCCAL INFECTION

- Ceftriaxone, 50 mg/kg to a maximum of 125 mg as a single IM injection OR
- Cefotaxime, 25mg/kg IV OR IM every BID to TID for 7 days OR
- Penicillin G Sodium Crystalline, 50,000 IU/kg QID for 10 days
- N.B. Most gonococcal strains are now resistant to penicillin.

PROPHYLAXIS OF GONOCOCCAL CONJUNCTIVITIS

- Clean the newborn's eye with 0.9 % saline or clean water using sterile gauze
- Apply single strip of ointment into each eye any of the above antibiotic eye ointments

Referral: In severe and complicated cases refer to an ophthalmologist

19.3 BLEPHARITIS

BRIEF DESCRIPTION:

- Blepharitis is a general term for inflammation of the eyelid margins
- It is one of the most common causes of external ocular irritation
- It is usually chronic and bilateral
- If it is associated with conjunctivitis, it is termed Blepharoconjunctivitis
- There are three types of blepharitis: Seborrhoeic, Staphylococcal and demodectic
- Patients should be advised that a permanent cure is unlikely, but control of symptoms is usually possible

STAPHYLOCOCCAL (ULCERATIVE) BLEPHARITIS

BRIEF DESCRIPTION:

- The most common causes of blepharitis, usually caused by staphylococcus aureus
- It is more common in younger individuals

CLINICAL FEATURE:

Symptoms

- Irritation and burning to peak in the morning and improve as the day progresses
- Foreign body sensation, itching, and crusting, particularly upon awakening

Signs

- Hard, brittle fibrinous scales and hard, matted crusts surrounding individual eyelash ('collarettes") on the anterior eyelid margin
- Ulceration of anterior eyelid margin
- Injection and telangiectasia of anterior and posterior eyelid margin
- White lashes (Poliosis) & loss of eyelashes (madarosis)
- Trichiasis can be seen in varying degrees depending on the severity and duration

Investigation & diagnosis: clinical

TREATMENT

Goals of treatment

- To alleviate the symptoms
- To prevent losses of eye lashes
- To correct trichiasis and prevent blindness

Non-pharmacological treatment

- Eyelid hygiene (see under Seborrhoeic blepharitis)
- Surgical correction of trichiasis

PHARMACOLOGICAL TREATMENT

Topical

- Dexamethasone eye drop, 1 drop 4 to 6 times per day, for 3 to 6 weeks, then taper every 5 to 7 days OR
- Oxytetracycline + Polymyxin B +Hydrocortisone suspension, apply 1 drop BID to TID, for 2 to 4 weeks OR
- Neomycin + Polymyxin B Sulphate + Dexamethasone suspension, apply 1 drop BID to TID, for 2 to 4 weeks OR
- Tetracycline 1% ointment, apply single strip BID to TID, for 2 to 4 weeks

OR

- Erythromycin 0.5% ointment, apply single strip BID to TID, for 2 to 4 weeks

Systemic (for recurrent cases)

- Doxycycline 50 to 100mg PO BID for 1 week, then daily for at least 6 weeks OR
- Tetracycline 250mg PO QID for 6 weeks, then tapered slowly OR
- Azithromycin 500 mg PO daily for 3 days, with 1-week 3 cycles OR

NB. Topical and systemic medications should be given simultaneously. Tetracycline should not be used in children under the age of 12 years or in pregnant or breastfeeding women.

Additional

- Artificial tears for dryness TID to 5 time per day depending on severity

Referral: In severe and complicated cases refer to an ophthalmologist

SEBORRHOEIC BLEPHARITIS

BRIEF DESCRIPTION:

- The inflammation is located predominantly at the anterior eyelid margin
- Meibomitis is a form of seborrheic blepharitis in the posterior eyelid margin
- In one third patients there is aqueous tear deficiency (dry eye)
- It may occur alone or with staphylococcal blepharitis

CLINICAL FEATURES

Symptoms

- Chronic eyelid redness, burning, foreign body sensation, itching
- A variable amount of oily or greasy crusting, eye discharge
- Easily applicable eyelashes

Signs

- Dandruff-like flakes "scurf" randomly distribute on and around eyelashes

Investigation & diagnosis: Clinical

TREATMENT

Goal of treatment

- To alleviate the symptoms

Non-pharmacological Treatment

- Eyelid hygiene, which includes
- Warm compression with clean towel for up to 10 minutes daily to TID
- Massaging or expression of meibomian gland secretions
- Scrub: cleanliness of the eyelid margins to remove keratinized cells and debris with baby shampoo, tea water, salt water or commercially available eyelid scrub

PHARMACOLOGICAL TREATMENT

- **Oxytetracycline + Polymyxin B +Hydrocortisone suspension**, apply 1 drop BID to TID, for 2 to 4 weeks OR
- **Neomycin + Polymyxin B Sulphate + Dexamethasone suspension**, apply 1 drop BID to TID, for 2 to 4 weeks OR
- **Tetracycline 1% ointment**, apply single strip BID to TID, for 2 to 4 weeks OR
- **Erythromycin 0.5% ointment**, apply single strip BID to TID, for 2 to 4 weeks

DEMODECTIC BLEPHARITIS

BRIEF DESCRIPTION

- It caused by infestation of the eyelash follicles with a mite, Demodex folliculorum

- Milder form of blepharitis, with little or no inflammation
- Can cause both anterior and posterior blepharitis
- Overpopulation or hypersensitivity the mite may lead to symptoms

CLINICAL FEATURES

Symptom

- Generally asymptomatic
- Symptomatic if the organisms elevated and causes frequent chalazion, hordeola or madarosis

Sign

- Waxy, cylindrical cuffs or "sleeves" around the basis of the eyelashes
- Mites can be demonstrated under ×16 slit lamp magnification

Investigation and diagnosis: clinical

TREATMENT

Goal of treatment

- To treat the infestation and symptomatic relieve

Non-pharmacological treatment

- Eyelid hygiene to prevent reproduction (see under seborrheic blepharitis)

Pharmacological treatment

- Ivermectin topical (1% cream) 2 times 1-week apart OR
- Ivermectin oral two doses of 200 µg/kg 1 week apart

19.4 CELLULITIS

PRESEPTAL CELLULITIS

Brief description:

- An infection of the subcutaneous tissues anterior to the orbital septum, the globe and orbit are not involved
- It usually results from inoculation following trauma or skin infection
- S. aureus and streptococci are the most common organisms, H. influenzae should, however, be considered in children under five years old
- Suspect anaerobes if a foul-smelling discharge or necrosis is present or there is a history of animal or human bite
- Consider viral if there is skin rash (herpes simplex or herpes zoster)
- Preseptal cellulitis in infants and children under age 5 may be associated with bacteremia, septicemia, and meningitis

CLINICAL FEATURES

Symptoms

- Eyelid swelling & redness, pain, low grade fever, irritability

Signs

- Eyelid erythema, edema, ptosis, warmth (may be quite dramatic)
- Visual acuity is normal and full ocular motility without pain

Investigation & diagnosis

- CBC with differential, gram stain, culture (pus, blood)

TREATMENT

Goals of treatment

- To reduce pain
- Treat infection
- Prevent complications

Non-pharmacological treatment

- Warm compression to affected area TID
- Consider incision and drainage if there is an abscess

PHARMACOLOGICAL TREATMENT

Mild Preseptal Cellulitis

- **Amoxicillin/clavulanate 250 to 500** mg PO TID for 10 days (for children 20 to 40 mg/kg/day into 3 divided dose) OR
- **Trimethoprim/Sulphamethoxazole 160mg/**800mg PO BID for 10 days (for children 8mg/40mg/kg/day, into 2 divided doses) OR
- **Erythromycin 250 to 500mg** PO QID for 10 days (for children 30 to 50mg/kg/day into 3 to 4 divided doses)

Moderate to severe Preseptal cellulitis:

- **Ceftriaxone 1gm** IV BID 10 to 14 days (for children 40mg/kg/day IV in 2 divided doses) PLUS Gentamicin 2.0mg/kg IV loading dose, then 1mg/kg IV TID for 10 to 14 days OR
- **Clindamycin 300mg** IV QID for 10 to 14 days (for children 1mg/kg/day IV into 4 divided dose) PLUS Gentamicin 2.0mg/kg IV loading dose, then 1mg/kg IV TID for 10 to 14 day

NB. IV antibiotics can be changed to comparable oral antibiotics after significant improvement.

Refer: In severe and complicated cases, refer to an ophthalmologist

ORBITAL CELLULITIS

BRIEF DESCRIPTION:

- Active infection of the orbital soft tissue posterior to the orbital septum
- It can occur at any age but is more common in children, there is commonly a recent history of nasal, sinus or respiratory symptoms
- In more than 90% of cases occurs as a secondary extension of bacterial sinusitis

- Delay in treatment may result in progression to cavernous sinus thrombosis
- Blindness, cranial nerve palsies, brain abscess, and even death can result and best avoided by aggressive management
- Streptococcus pneumoniae, Staphylococcus aureus, Streptococcus pyogenes and Haemophilus influenzae are common causative organisms

CLINICAL FEATURES:

Symptoms

- Red eye, pain, fever, headache
- Blurred vision, double vision(diplopia)
- Lid swelling, "bulging" eye

Signs

- Decreased visual acuity, impaired color vision and pupillary abnormality
- Lid erythema, edema and tenderness, conjunctival edema (chemosis)
- Non axial proptosis and painful ocular movement with restricted motility
- Choroidal folds and optic disc swelling may be present on fundus examination

INVESTIGATION & DIAGNOSIS

- CBC with differentials, blood culture
- X-ray of paranasal sinuses
- CT Scan/MRI
- Lumbar puncture if meningeal signs develop

TREATMENT

Goals of treatment

- Reduce pain

- Treat the infection
- Prevent both sight- & life-threatening complications

Non-pharmacological treatment

- Orbitotomy for subperiosteal abscess drainage if indicated
- Drainage of infected sinus in cases of severe sinus diseases
- Severe optic nerve compression may warrant an emergency canthotomy/ cantholysis

PHARMACOLOGICAL TREATMENT

- Triple therapy: Ceftriaxone 1gm IV BID + Cloxacillin 500 mg IV QID + Metronidazole 500 mg IV TID for up to 4 days of apyrexia
- When orbital cellulitis is consistently improving, the regiment can be changed to oral antibiotics to complete the 14-day course - Amoxicillin/ clavulanate 250 to 500 mg po TID

ADDITIONAL

- Nasal decongestants
- Tetracycline or Chloramphenicol or Erythromycin, single strip ointments applied QID for corneal exposure if there is severe proptosis
- N.B. Refer: In severe and complicated cases, refer to an ophthalmologist

19.5 DACRYOADENITIS AND DACRYOCYSTITIS

DACRYOADENITIS

BRIEF DESCRIPTION:

- It is an infection of the lacrimal gland, typically occurs in children and young adults

- Usually caused by virus (mumps, infectious mononucleosis, influenza, herpes zoster) or idiopathic, rarely by bacteria (Staphylococcus aureus, Neisseria gonorrhea, streptococci)
- Chronic conditions such as sarcoidosis, Sjogren syndrome, thyroid disease and some chronic infections usually give a less acute onset and involvement can be bilateral

ACUTE DACRYOADENITIS

Clinical features:

Symptoms

- Unilateral pain, redness and swelling of outer one-third of upper eyelid
- Often there will be tearing & eye discharge

Signs

- Erythema, warmth & tenderness over outer one-third of upper eyelid
- May find hyperemia of palpebral lobe of lacrimal gland

Investigation and diagnosis:

- CBC, Gram's stain, culture (pus or blood)

TREATMENT

Goal of treatment

- Alleviate the pain
- Treat the infection for bacterial infections
- Shorten the course of the diseases for viral infections

Non-pharmacological treatment

- Incision and drainage if there are an abscess
- Cold compresses to the area of swelling and tenderness

PHARMACOLOGICAL TREATMENT

BACTERIAL OR INFECTIOUS (BUT UNIDENTIFIED) ETIOLOGY

Mild to moderate

- **Cloxacillin 500mg** PO QID for 7 to 14 days (for children 50 to 100mg/kg/day in 4 divided doses) OR
- **Amoxicillin/clavulanate 625mg** PO BID for 10 to 14 days (for children 20 to 40mg/kg/day into 3 divided dose) OR
- **Cephalexin 250 to 500mg** Po QID for 7 to 14 days (for children 25 to 50mg/kg in 4 divided doses)

Moderate to severe:

Admit to hospital, IV antibiotic (see under Dacryocystitis)

N.B. The antibiotic regimen should be adjusted according to the clinical response and the result of culture and sensitivity. IV medications can be changed to oral depending on the rate of improvement of the patient.

Viral (mumps, infectious mononucleosis) supportive

- **Acetaminophen 1000mg** PO every 4 to 6 hours for adults (pediatric dose: 10 to 15 mg/kg/dose three to four times a day)
- Ibuprofen 400mg PO TID to QID

DACRYOCYSTITIS

BRIEF DESCRIPTION:

- An inflammation or infection of the lacrimal sac, usually secondary to obstruction of NLD
- Chronic tear stasis and retention lead to secondary infection with bacteria, most commonly staphylococcal or streptococcal
- There may be associated Preseptal cellulitis
- Fistula formation, lacrimal sac cyst or mucocele can occur in chronic cases

ACUTE DACRYOCYSTITIS

CLINICAL FEATURE:

Symptoms

- Pain, redness & swelling over the lacrimal sac, tearing, eye discharge

Signs

- Erythematous, tenderness on nasal aspect of lower eyelid

Investigation & diagnosis:

- Gram's stain, pus culture

TREATMENT

Goal of treatment

- Relieve pain
- Cure the infection
- Open the drainage and reduce tearing

Non-pharmacological treatment

- Warm compresses and gentle massage to the inner canthal region QID
- Incision and drainage of a pointing abscess
- Dacryocystorhinostomy (DCR) for chronic Dacryocystitis, once the acute episode has resolved

PHARMACOLOGICAL TREATMENT

Mild

- Cloxacillin 500mg PO QID for 10 to 14 days (for children 50 to 100mg/kg/day in 4 divided doses) PLUS Chloramphenicol eye drop, 1 drop QID for 10 to 15 days OR
- Amoxicillin/clavulanate 625mg PO BID for 10 to 14 days (for children 20 to 40mg/kg/day into 3 divided doses) PLUS Gentamicin eye drop, 1 drop QID for 10 to 15 days

MODERATE TO SEVERE: HOSPITALIZE AND TREAT WITH IV MEDICATIONS

- Cephazolin Sodium 1gm IV TID for 10 to 14 days (for children 25 to 100mg/kg/day into 3 divided doses) OR
- Cefuroxime 750mg IV TID for 10 to 14 days (for children 50 to 100mg/kg/day IV into 3 divided doses) OR
- Clindamycin 300mg IV QID for 10 to 14 days (for children 1mg/kg/day IV into 4 divided doses)

PLUS

- Gentamicin 2.0mg/kg IV loading dose, and then 1 mg/kg IV TID for 10 to 14 days
- NB. N.B. IV antibiotics can be changed to comparable oral antibiotics after significant improvement is observed.

Referral: in severe and complicated cases refer to an ophthalmologist

19.6 SWELLING ON AND AROUND THE EYEBALL

HORDEOLUM

INTERNAL HORDEOLUM

BRIEF DESCRIPTION:

- It is secondary infection of inspissated meibomian glands caused by staphylococcus
- It can be quite severe because the pus cannot drain away easily
- Occasionally, the inflammation may spread to the orbit, causing cellulitis
- More common in adolescent and young adult

CLINICAL FEATURES:

Symptoms

- Eyelid lump/swelling, pain

Signs

- Eyelid erythema & tenderness
- Visible or palpable, well-defined subcutaneous nodule within the eyelid tarsus
- Enlarged preauricular lymph nodes

Investigation & diagnosis: clinical

TREATMENT

Goals of treatment

- Reduce the pain and swelling
- Cure the infection

Non-pharmacological treatment

- Warm compresses; applied for 10 minutes twice daily for 2 to 4 weeks
- Incision and drainage if there is an abscess
- Incision and curettage if not disappear with other treatments

Pharmacological treatment

- **Cloxacillin 50mg/kg** PO in four divided doses for 7 days OR
- **Ampicillin 50 mg/Kg** PO in four divided doses for 7 days

EXTERNAL HORDEOLUM (STYE)

BRIEF DESCRIPTION:

- Acute small staphylococcal abscess of an eyelash follicle and glands of Zeis
- Common in children and young adult
- Solitary or multiple and occasionally minute abscesses may involve the entire lid margin
- In severe cases a mild Preseptal cellulitis may be present

CLINICAL FEATURES:

Symptoms

- Painful swelling of eyelid margin of short duration

Signs

- Visible or palpable, tender well-defined nodule in the eyelid margin

Investigations and diagnosis: Clinical

TREATMENT

Goal of treatment

- Reduce the pain and swelling
- Treat the infection

Non-pharmacological treatment

- Warm compresses, applied for 10 minutes twice daily for 2 to 4 weeks
- Epilation of the involved eyelashes
- Incision and curettage if other treatments failed
- NB. No pharmacological treatment is needed most cases, styes frequently resolve spontaneously or discharge anteriorly. If it is not resolved spontaneously

PHARMACOLOGICAL TREATMENT

- Oxytetracycline + Polymyxin B + Hydrocortisone, 1 drop BID to TID for 2 to 4 weeks OR
- Neomycin Sulphate + Polymyxin B + Dexamethasone, 1 drop BID to TID for 2 to 4 weeks OR
- Tetracycline 1% ointment, single strip apply BID to TID for 2 to 4 weeks OR
- Erythromycin 0.5% ointment, single strip apply BID to TID for 2 to 4 weeks

If there is associated preseptal cellulitis add

- Ampicillin 50mg/kg PO in four divided doses for 7 days OR
- Cloxacillin 50mg/kg PO in four divided doses for 7 days

MEIBOMIAN CYST (CHALAZION)

BRIEF DESCRIPTION:

- It is a sterile chronic granulomatous inflammatory lesion (lipogranuloma) of the meibomian, or sometimes Zeis, glands caused by retained sebaceous secretions
- Patient with acne, rosacea or Seborrhoeic dermatitis are at increased risk of chalazion formation, which may be multiple or recurrent.
- A recurrent chalazion should be biopsied to exclude a masquerading malignancy

CLINICAL FEATURES:

Symptom

- Gradually enlarging painless rounded lump

Sign

- Nontender visible or palpable, well-defined nodule in the eyelid within the tarsal plate
- Bulging inspissated secretions may be visible at the orifice of the involved gland
- Eversion of the lid may show an associated polyploidy granuloma

Investigation & diagnosis: Clinical

TREATMENT

Goal of treatment

- Remove the lump/nodule from the eyelid

Non-pharmacological treatment

- Hot compress several times daily

- Incision and curettage, suture should not be used

PHARMACOLOGICAL TREATMENT

- Antibiotics if there is bacterial infections
- Topical antibiotic is used three times daily for 5 days following curettage
- Systemic tetracycline may be required as prophylaxis in patients with recurrent chalazia, particularly if associated with acne rosacea

N.B. If the chalazion is recurrent, refer the patient to an ophthalmologist for further management to rule out malignant lesion like **Sebaceous Gland Carcinoma**

PINGUECULA AND PTERYGIUM

PINGUECULA

BRIEF DESCRIPTION:

- Extremely common asymptomatic elastotic degeneration of the conjunctival stroma.
- It is more frequently located at the nasal than the temporal limbus, but is frequently present at both
- The cause is believed to be actinic damage, similar to the etiology of pterygium
- The distinction is that the limbal barrier to extension has remained intact with a pinguecula, though transformation can occur

CLINICAL FEATURES:

Symptoms

- Usually, asymptomatic
- Occasionally a pinguecula may become acutely inflamed (pingueculitis)

Signs

- Yellow–white mound or aggregation of smaller mounds is seen on the bulbar conjunctiva adjacent to the limbus

Investigations & diagnosis: Clinical

TREATMENT

Goal of treatment

- To relive symptoms if symptomatic
- Cosmetic reasons

Non-pharmacological

- Excision for cosmetic reasons or significant irritation (with low recurrence rate)
- Thermal laser ablation can be effective

Pharmacological treatment

- Topical lubrication for irritation
- Topical steroid, short course, for pingueculitis

Pterygium

Brief description:

- A triangular fibrovascular subepithelial ingrowth of degenerative bulbar conjunctival tissue over the limbus onto the cornea
- The condition tends to run in families, AND histologically similar to a pinguecula
- Shows elastotic degenerative changes in vascularized subepithelial stromal collagen

CLINICAL FEATURES:

Symptoms

- Most small lesions are asymptomatic
- Irritation and grittiness
- Lesions may interfere with vision

Signs

- Three parts: a ‘cap’ (an avascular halo-like zone at the advancing edge), a head and a body
- Grading

Investigations and diagnosis: Clinical

TREATMENT

Goal of treatment

- Symptomatic relieve
- Cosmesis, it may be a significant problem for individual

Non-pharmacological treatment

- Sunglasses to reduce ultraviolet exposure
- Correction of refractive error (astigmatism) with spectacles
- Simple excision (high rate of recurrence, with often with more aggressive behavior than the original lesion)

PHARMACOLOGICAL TREATMENT

- See under pinguecula

19.7 REFRACTIVE ERROR AND LOW VISION

REFRACTIVE ERROR

BRIEF DESCRIPTION:

- Types - myopia (shortsightedness), hypermetropia (farsightedness), astigmatism and presbyopia.
- Early referral, especially in children with squint or abnormal pupillary light reflex

- It affects children in school's performance, adult above 45 years(presbyopia) in reading

CLINICAL FEATURE:

Symptom

- Distant or near decreased vision
- Eyestrain(asthenopia), frontal headache, squint

Sign

- Improving visual acuity with pinhole test
- Inappropriate reading distance (far or near)

Investigation and diagnosis

- Clinical refraction – measures type and degree of refractive error

TREATMENT

Goal of treatment

- To prevent the development of amblyopia (lazy eye) in children
- To correct the refractive error to improve quality of daily activities

Non-pharmacological treatment

- Prescribe spectacles or contact lens (by optometrist or ophthalmologist)
- Refractive surgery is the last option for correction of refractive error

Pharmacological treatment

- None

LOW VISION

Brief description:

- Clinically defined as best corrected vision (BCV) < 6/18 to light perception (LP) in better eye, it used for service provision

- Epidemiologically defined as BCV < 6/18 to 6/60 or central visual field < 20o, it used for common understanding in research
- It is common disorder affection old age group and age-related macular degeneration (AMD) is the most common cause of low vision

CLINICAL FEATURES:

Symptoms

- Reduction in vision unamenable to standard correction

Signs

- Visual acuity < 6/18 in better eye, after standard correction

Investigations and diagnosis:

- Clinical

TREATMENT

Goal

- Rehabilitation with low vision aid

Non-pharmacological

- Optical: special spectacles, magnifiers, telescope
- Assisting device: cane - mobility, Typoscope – writing, brighter illumination

Pharmacological

- None

Referral: Referral to low vision center or tertiary eye care center

FURTHER READING

1. Kanisk's Clinical Ophthalmology, 9th Edition, John F. Salmon, 2020
2. Eye Diseases in Hot Climates, 4th Edition, John Sandford- Smith, 2014
3. Basic Clinical and Science Course series, American Academy of Ophthalmology, 2019 – 2020

19.8 FORTIFICATION OF ANTIBIOTICS

- Instruction for preparation of fortified antimicrobial eye drops
- General Instructions
    - Should be prepared under aseptic condition by qualified professional
    - Disposable syringe should be used
    - All drops should be labeled for name of antibiotic drop, date of preparation and date of expiry, frequency of application and need to be kept refrigerated etc.
- **Aminoglycosides**
    - **Fortified Tobramycin/ Gentamicin:** 15mg/ml (1.5%)
    - **Method:** Add 2 ml of parenteral antibiotics of tobramycin/Gentamicin (40 mg/ml) to 4ml of commercially available aminoglycoside eye drops (0.3%).
    - **Shelf Life:** 1 week in refrigerator at 4 degrees and 4 days in room temperature
- **Cephalosporin**
    - **Fortified Cefazolin/ Ceftazidime/ Ceftriaxone Eye Drops:** 50mg/ml (5%)
    - **Method:** Parenteral Cephalosporin 500mg is diluted with 2.5 ml sterile water/ balanced salt solution (BSS) and added to 7.5 ml of artificial tears
    - **Storage:** Refrigerate in 4 degrees Centigrade.
    - **Shelf Life:** 1 week in refrigeration at 4 degrees C and 4 days in room temperature
- **Fortified Vancomycin Eye Drops:** 50mg/ml (5%)
    - **Method: Vancomycin 500mg** powder is diluted with 2.5 ml sterile water/BSS and added to 7.5 ml of artificial tears
    - **Storage:** Refrigerate at 4 Degrees C.
    - **Shelf Life:** up to 28 days at 4 Degrees C

CHAPTER 20:

EAR, NOSE AND THROAT DISEASE

20.1 EAR CONDITIONS

ACUTE OTITIS MEDIA

BRIEF DESCRIPTION

- Acute otitis media is the rapid onset of signs and symptoms of inflammation of the middle ear cleft mostly following URTIs.
- The most common causative bacterial organism are Streptococcus Pneumonia, Haemophilus Influenza A and Moraxella catarrhalis. Viral infection, commonest etiologies, may commonly prepare the way for secondary bacterial infection.
- The younger the child, the more severe the generalized symptoms are and the more discrete the local signs are. On occasions, the gastrointestinal symptoms are the most pressing.
- **Risk factors:** crowed conditions, day care, passive smoking, bottle feeding, low socioeconomic status,

CLINICAL FEATURES

Symptom

- Symptoms vary according to patients' age
- Neonates only present with irritability and/ or feeding difficulty
- Infants and older children can present with fever (with or without prior history of URTI) and otalgia, or tugging on the ear.
- In severe cases, rigors and occasionally meningismus can occur in children.
- Adults and older children can present with otalgia (mostly worse by night),

sometimes fever and impaired hearing.

- Both adults and children can present with ear discharge lasting <2 weeks Pain often improves after the onset of discharge.

Signs

- Otoscopy shows hyperemia, bulging and opacity of the surface of tympanic membrane,
- Perforation of the tympanic membrane can be seen in advanced case mostly in the posterior quadrant of the tympanic membrane.
- Pneumatic Otoscopy can be performed to asses for tympanic membrane mobility.

Investigation and Diagnosis

- The Diagnosis of acute Otitis media is mostly clinical.

Additional tests

- Ear swab for culture and sensitivity

TREATMENT

Goal

- Relieve symptoms or pain
- Return hearing to normal
- Prevent chronicity and complications (like perforation, meningitis, brain abscess, etc).

Non pharmacologic

- Advise on keeping the ear dry. I.e. apply Vaseline soaked cotton during bathing.

Pharmacologic treatment

First line

- Pediatrics:Amoxicillin high dose 80-90 mg/kg/day po divided every 12 hour or every 8 hours for 10 days. (Adult: 1000mg BID or TID for 7 to 10 days)

Alternative, for non-responders to Amoxacillin

- Amoxicillin-clavulanate extra strength oral suspension 90/6.4 mg/kg/day po divided bid (preferred)

Second line drug

- **Ceftriaxone 50 mg/kg** IV or IM once daily x 3 days (is preferred in pediatrics), others agents in adults include: **cefuroxime axetil, cefpodoxime proxetil, cefixime**.
- If beta-lactamase allergy: **Azithromycin** 10 mg/kg per day orally (maximum 500 mg/day) as a single dose on day 1 and 5 mg/kg per day (maximum 250 mg/day) for days 2 through 5.

PAIN MANAGEMENT

- Paracetamol, 30-40mg/kg/24hrs in four divided doses to relieve pain. Alternative Ibuprofen

PREVENTION

- Parent education about risk factors
- Antibiotic prophylaxis – amoxicillin or macrolide shown effective at half therapeutic dose
- Pneumococcal and influenza vaccine
- Surgery: choice of surgical therapy for recurrent AOM depends on whether local factors (Eustachian tube dysfunction) are responsible (use ventilation tubes), or regional disease factors (tonsillitis, adenoid hypertrophy, sinusitis) are responsible

MASTOIDITES

BRIEF DESCRIPTION

- Poorly treated or untreated OM that last more than two weeks can lead to extension of the infection form mid era cavity to the mastoid air space leading to mastoiditis.

CLINICAL FEATURES

- Fever
- Profuse ear discharge
- Retro auricular swelling with tenderness

Investigations and diagnosis

- Culture and sensitivity tests

TREATMENT

Objective

- Eliminate the foci of infection in the temporal bone and the middle ear cavity.

Pharmacologic

- Patients with acute mastoidites should be admitted to the hospital and administered IV antibiotics active against resistant microorganisms, with bed rest and IV fluid. If not Acute mastoidites, it should be referred within 48 hours. Antibiotics should be considered with non-pharmacologic managements like drainage and surgery.
- If it is sub-per-ostial abscess, abscess drainage should be considered and referred for definitive management (cortical mastoidectomy)

ANTIBIOTICS FOR ACUTE MASTOIDITES

- If no recurrent AOM or no recent antibiotic use (3 to 6 months),
- **Vancomycin (15 mg/kg** intravenously [IV] every 6 hours; maximum 1 g per dose)
- If recurrent AOM (most recent episode within six months) or recent antibiotic administration,
- **Vancomycin PLUS Ceftazidime/cefepime 50 mg/kg** per dose IV every 8 hours (maximum 2 g per dose)

DURATION OF ANTIMICROBIAL THERAPY:

- Totally four weeks IV treatment may be continued for 7 to 1o days or IV to PO conversion should be done approximately after a clinical improvement.

Non pharmacologic

- Surgery if the inflammation is no longer confined to the mucosa but has extended to the bone

Prevention

- Early, adequate treatment of acute otitis media (AOM)
- Preventing recurrent AOM
- Immunization with the pneumococcal conjugate vaccine

Chronic Suppurative Otitis Media

- Chronic otitis media is defined as long-standing inflammation of the middle ear cleft in which characterized by chronically discharging ears for > 12 weeks (3 months).

CLINICAL FEATURES

Symptoms

- Constant or intermittent discharge (usually odorless) from the ear mostly not accompanied by otalgia.
- Hearing impairment in the affected ear

Signs

- Otoscopy: Tympanic membrane Perforation
- Tuning fork test (Rhinee and Webers Test): Conductive Hearing Loss
- Symptoms of impending complications like fever, lethargy, headache, vomiting, neck pain, changing mentation, dizziness, vertigo).

Investigations

- Culture of the ear discharge.

Treatment

Goals

- Keep the ear dry
- Eliminate the foci of infection in the temporal bone and the middle ear
- Construct the sound–conducting apparatus.

Non pharmacologic

- Instruct patients to keep the ear dry (Vaseline gauze, dry it after showering)
- Aural toilet (recommended together with topical antibiotics)

Pharmacologic

N.B. In acute exacerbations only Antibiotic treatment, whenever possible, must be directed by the results of culture and sensitivity of the ear discharge.

First line

Topical:

- **Ciprofloxacin ear drop**, 0.3%, 5ml. 2 – 3 drops twice daily for 02 weeks.
- N.B; Ciprofloxacin and other quinolone like Norfloxacin or Ofloxacin with or without steroid combination can be used,
- If initial topical antibiotic therapy failed: culture directed systemic therapy should be tried (refer if no microbiology laboratory).
- **Refer** patients to ENT specialists for

Prevention

- Cornerstone of therapy
- Promptly and appropriately treating AOM
- Strict water precautions for prevention and management of recurrence
- Education on the risk factors like passive smoke exposure, contaminated water, and malnutrition might help.

OTITIS EXTERNA

- Otitis External diffuse inflammation of the external ear canal which may involve the pinna or the tympanic membrane.
- The most common causative agents being Pseudomonas A., Staphylococcus aureus and other gram-negative microbes occurring as a polymicrobial infection.
- Fungal otitis external can occur in the setting of repeated antibiotic use.
- Frequent Swimming, Rigorous ear cleaning, excessive use of air phone and underlying dermatological conditions can be risk factors for otitis externa

ACUTE OTITIS EXTERNA

CLINICAL FEATURES

Symptoms

- Itching and Pain aggravated by movement and pressure on the auricle
- Rarely mucoid ear discharge
- Hearing impairment and aural fullness
- Posterior auricular lymphadenopathy

Signs

- Tragal tenderness,
- Otoscopic tenderness
- Erythematous and inflamed external ear canal,
- Posterior auricular Lymphadenopathy
- Diffuse edema of the External ear canal, with apparent granulation tissue and trisumus should alert the health care worker to consider malignant Otitis externa (Skull Base Osteomellitus) and seek immediate referral.

INVESTIGATIONS AND DIAGNOSIS

- Diagnosis of Otis external is clinical

- Culture and sensitivity studies can be mandated in recurrent cases and those unresponsive to antibiotics.

TREATMENT

Goal

- To relive pain and other symptoms
- To treat the infection
- To prevent complications

Non-pharmacologic treatment

- Keep the ear dry
- Clean the ear until dry with ear wicks or suction if available cotton wicks by the physician

PHARMACOLOGIC TREATMENT

First line

- **Ciprofloxacin 0.2% and dexamethasone 0.1%** otic suspension 2 – 3 drops twice daily for a total of 02 weeks (better tolerability).

OR

- **Neomycin 0.35%, Polymyxin B 10,000 units/mL,** and **hydrocortisone 0.5%** otic solution2 – 3 drops twice daily for a total of 02 weeks.

NB; Apply ear wicks to keep the external ear canal open for the first 3 days in diffusely edematous and narrow canal. Mild cases with only minor discomfort and pruritus, non-antibiotic topical preparation containing an acidifying agent and a glucocorticoid (eg,Acetic acid 2% and hydrocortisone 1% otic solution) can be used. Avoid use of acidifying antiseptic agents if tympanic membrane is perforated.

- Aminoglycoside topical solutions can be used when ciprofloxacin and other quinolone are not available however avoid usage in perforated tympanic membranes due to ototoxicity.

- Systemic antibiotic (in addition to topical) can be considered in severe cases and when Malignant OE is suspected (IV antibiotics recommended), immunosuppression, regional lymphadenopathy, systemic symptoms like fever until patient can be referred.

CHRONIC OTITIS EXTERNA

- Usually caused by vegivores ear cleaning or total absences of ear wax. The cause can be infectious (bacterial or fungal) or non-infectious.

CLINICAL FEATURES

Symptom

- Long standing ear itching

Sign

- Dry, wide external oditerium mities with complete absence of wax (non-infectious)
- Hypertrophic external olitory canal or Fungal Hyphae can be seen in the canal in cases of otomycosis.

TREATMENT

Non-infectious

Non-pharmacologic:

- Acidifying agents like acetic acid
- Treat the underling conditions like
- applying cerumenolytic agent's alcohol, glycerin
- dermatologic conditions

For infectious

- Topical antifungals with cleaning or debridement

CERUMEN (WAX) IMPACTION

BRIEF DESCRIPTION

- Ear wax is a mixture of secretions from ceruminous and sebaceous glands, epithelial debris and dust.
- Ear wax is part of the body physiological defense mechanisms and needs removal only when it is symptomatic.

CLINICAL FEATURES

- Aural fullness, Itching and decreased hearing.
- Occasionally tints, vertigo
- Otoscopy can reveal wax obliterating the ear canal.

TREATMENT

- Cerumenolytic drops like Hydrogen per oxide, Olive oil
- Syringing or manual irrigation (contraindications like previous history of ear discharge/tympanic membrane perforation, previous history of ear surgery, the only hearing ear). The only and rare complication of syringing is tympanic membrane perforation. It can be managed in a conservative way by advising the patient to keep the ear dry and distance themselves from other individuals with upper respiratory infections. NB traumatic tympanic membrane perforation usually heals by itself with conservative management.
- Manual removal by an expert

N.B., Syringing and manual irrigation should be done by a Luke warm water (body temperature, 37 degree Celsius) and whenever possible after the usage of ceruminlytics for 2-3 days.

FOREIGN BODIES IN THE EAR

BRIEF DESCRIPTION

- The majority of patients with foreign bodies in the ear are children.
- The organic or inorganic objects may give rise to otitis externa (especially

organic) by local irritation of the epithelium of the mental walls.

CLINICAL FEATURES

- Any suspicion for foreign body
- Foreign body detected on Otoscopic examination.

INVESTIGATIONS

- Diagnosis is clinical

TREATMENT

Goals

- Open the ear canal which is completely or partially closed by removing the foreign body.
- Eliminate secondary infections

Non pharmacologic

- Irrigation of the suspected ear with water by ENT specialist if there is no perforation of the tympanic membrane.
- Cerails can be irrigated if fride, unfride Cerails should not be irrigated because it get swollen
- **N.B.** Foreign bodies that cannot be removed by irrigation should be removed manually, using general anesthesia in small children.
- Ears with vegetable foreign bodies should not be irrigated, since this may cause the matter to swell.
- Live insects can be killed rapidly by instilling alcohol, 2% lidocaine (Xylocaine), and Olive oil. Before removal is attempted.
- Inorganic foreign body especially lithium button battery should be removed urgently within 2 hours
- Manual removal is another approach.
- If the foreign body is in the middle ear early referral is advisable

TINNITUS

BRIEF DESCRIPTION

- An auditory meaningless perception in the absence of external source of sound, likely related to loss of stimuli to the central auditory pathways.
- (Meaning less perception in the absence of external auditory sound is tinnitus, If meaning full perception in the absence of external auditory sound is auditory hallucination)
- It can occur on 1 or both sides of the head.
- Mostly happens in the setting of Sensory Neural Hearing Loss (SNHL).
- Could be intermittent or persistent (> 6 month)
- Could be Primary or idiopathic and Secondary i.e with identifiable underlying cause)
- Could be subjective or objective
- Could be pulsatile or non-pulsatile
- Could be caused by local or systemic disease
- Could affect the patient's quality of life and lead to depression, anxiety and other mental health issues.

THE SOUNDS CAN BE EXPRESSED AS THE FOLLOWING MEANINGLESS SOUNDS

- Hissing, roaring Buzzing, tingling sounds in one or both ears
- Local causes
- It can have associated hearing Impairment, vertigo, aural fullness
- Any history of ototoxic drug intake

SYSTEMIC CAUSES

- Psychogenic: Associated mental health disturbances i.e sleep disturbance , emotional disturbances , anxiety , anger , frustration

- Organic: History of Diabetic, Hypertension and Dyslipidemia, neurologic disorders

Signs

- Examine for signs of inner, middle ear and external disease on Otoscopy i.e Tympanic membrane Perforation, Otorrhea, cerumen impaction, objective peripheral vertigo.
- Neurological examination
- Hear murmur, head and neck masses (carotid bruits), and Vascular sounds

Investigation and diagnosis

For local causes-

  - Hearing assessment is part of tinnitus evaluation
  - Tunning Fork test
  - Audiometric evaluation (to assess for the type and degree of hearing loss)
  - Imaging Studies only when underlying organic lesion is suspected or pulsatile tinnitus.
  - Workup for systemic causes (CBC, VDRL, thyroid function test, Doppler ultrasound, etc)

TREATMENT

Non-pharmacologic

- Avoid ototoxic medications
- Treat underlying cause if identified
- Provide counseling for patients with bothersome symptoms and if needed psychiatric evaluation and treatment.
- Recommend Hearing Aids for individuals with hearing impairment (N.B; Hearing aids should be encouraged even for elderly patients as its improves their quality of life greatly)

- Educate patients that there is no established cure for tinnitus, advantages of sound therapy like playing the radio, CD and MP3 players especially during the night time.

PHARMACOLOGIC

- Treat underling case, if any

20.2 NOSE AND PARA-NASAL SINUSES

20.2.1 RHINO SINUSITIS

ACUTE RHINO SINUSITIS

- Acute rhinosinusitis may include viral, bacterial and allergic rhinites.

COMMON COLD (VIRAL RHINITIS)

Brief Description

- Also known as Upper Respiratory Tract Infection is a common acute illness
- Symptoms are self-limiting often lasting up to 10 days
- Transmission occurs through droplets

Symptoms

- Fever usually low grade
- Nasal congestion, Rhinorrhea,
- Sore throat, cough, general malaise

Investigation and Diagnosis

- The diagnosis of common cold should be made clinically yet it is important to distinguish it from other illnesses with similar symptoms.

TREATMENT

Goals

- Reduction of symptom duration and severity

Non pharmacologic

- Bed Rest
- Adequate Hydration
- Steam

Pharmacologic

- Symptomatic Treatment: Paracetamol or NSAID
- Topical decongestants
- Oral Antihistamines

(Dosage can be used as mentioned on other parts of the guideline)

N.B: Avoid usage or antibiotics for patients with common cold.

ACUTE BACTERIAL RHINOSINUSITIS

BRIEF DESCRIPTION

- Non-resolving acute viral rhinosinusitis with 10 days or worsening of symptoms after 5 days. 2% of acute viral rhinosinusitis can complicate with bacterial rhinosinusitis.
- The most frequently occurring micro-organisms are Haemophilus influenza, Streptococcus pneumococcus and Moraxella catarrhalis.
- Dental origin can be caused by extension of a periapical inflammation or abscess.

CLINICAL FEATURES

Symptoms

MAJOR SYMPTOMS

- Purulent Nasal discharge (anterior or posterior/or post nasal drip)
- Anosmia, hyposmia,
- High grade fever
- Sinus tenderness
- Nasal obstruction

MINOR SYMPTOMS

- Low grade fever
- Dental Pain, Pressure/ Fullness in the face and the head or both.

Additional symptoms

- maxillary dental pain
- Systemic symptoms like fever, malaise

Signs

- Palpable tenderness of the cheeks and the sinuses, percussion tenderness of the upper teeth
- Purulent discharge in the nose or posterior pharynx

INVESTIGATIONS AND DIAGNOSIS

If there are two major symptoms or one major and two minor symptoms acute bacterial rhinosinusitis can be suspected. Investigations may include:

- Anterior and posterior rhinoscopy
- Naso endoscopy
- Radiography, possibly including a contrast medium
- CT scan (Signs of extra sinus involvement (orbital or facial cellulitis , Orbital Protrusion , abnormalities of eye movement , neck stiffness))

N.B The diagnosis of ABRS can be established via the presence of the three cardinal symptoms (Nasal discharge + Nasal Obstruction/ Facial Pain) and routine imagining is not advised.

TREATMENT

Objective

- Relieve symptoms
- Clear the infection and prevent complications (e.g., subdural empyema, epidural abscess, brain abscess, meningitis and cavernous sinus thrombosis)
- Avoidance of chronic sinus disease
- Avoidance of unnecessary antibiotic use.

Non pharmacologic

- Nasal Saline Irrigation
- Steam inhalation

Pharmacologic

First line

- **Amoxicillin,** children; 90 mg/kg/day PO divided every 12 hourly for 10 to 14 days; Audits; 1000 mg P.O., TID for 7days

Alternatives

If no improvement with amoxiciline or recent antibiotic use in the last 30 days.

- **Amoxicillin-Clavulanate,** children; suspension, 90 mg/kg/day (Amoxicillin component), PO divided every 12 hourly x 10 days; adults; 875/125 PO bid for 5 to 7 days or the extended release form 1000/62.5 mg 2 tabs or 2000/125 mg 1 tab, PO bid x 5-7 days

If penicillin allergy

- **Azithromycin**, children; 200mg/5ml P.O., daily for 3 days adults; 500mg P.O., daily for 3 days

ADJUNCT SYMPTOM RELIEF THERAPIES:

Xylometazoline hydrochloride 0. 05% or 0. 1%, 2 drops BID daily not recommended or used for < 3 days only (if used more than recommended it may cause rhinitis medecamenthosa)

LORATADINE,

Children 2-6 years; 1 teaspoonful once daily children over 6 years; 2 teaspoonful's P.O., daily adults; 10mg P.O., daily for 7 to 10 days.Antihistamines do have minor or no role unless definite underlying allergic rhinitis.

If there is no response with pharmacologic treatment, the patient can be referred for surgery.

ALLERGIC RHINITIS

BRIEF DESCRIPTION

- IgE mediated inflammatory response of the nasal mucous membrane after exposure to allergens.
- Can be seasonal or chronic and perennial
- Can occur with other auto immune diseases

CLINICAL FEATURES

Symptoms

- Itching of the nose, eye, ear and throat, nasal obstruction, sneezing attacks, A clear watery nasal discharge

If there is a headache and anosmia, it is an indication for sinus involvement

Signs

- Anterior rhinoscopy pale or bluish discoloration of the nasal mucosa and turbinates
- Watery eye discharge and red eye (if there is concomitant allergic

conjunctivitis)

- Allergic Shiner (Darkening and puffiness of the lower eye lids)
- Allergic crease across the nasal bridge (In chronic cases)

Investigations

- Diagnosis is clinical
- Allergic skin testing and IgE level tests can be done when possible.

TREATMENT

Goals

- Give symptomatic relief and improve the quality of life.

Non pharmacologic

- Avoid exposure to Known allergens
- Nasal saline / Salt water Irrigation.

Pharmacologic (symptomatic management)

First line

- If the predominant símpateme is congestión, decongestants can be used.
- If the dominant symptome is allergic, antihistaminies can be used.
- Xylometazolinee, adults; 1% 2 to 3 drops 2-3 times into each nostril daily; infants and small children; 0.5% 1 to 2 drops 1 – 2 times a day into each nostril

And/or

- **Cetirizine**, children below 12 years; 5 - 10 mg P.O., daily; children above 12 years and adults; 10mg tab P.O., daily

OR

- **Loratadine**, one tablet (10mg) once daily Syrup: two teaspoonful (10mg) once daily. body weight <30kg; 5ml [5mg], (one teaspoonful), once daily.

body weight >30kg; 10ml [10mg], (two teaspoonful), once daily.

OR

- **Dexchlorpheniramine maleate,** 6mg PO BID Syrup for adults and children12 years or older: one-half teaspoonful 3-4 times a day. For children 6-12 years of age: one-quarter teaspoonful 3 or 4 times a day for children 2-6 years of age

and/or

- **Momethasone Furate,** Children 2-11 years: 1 spray (50 mcg of Momethasone in each spray) per nostril once daily (total daily dose of 100 mcg);Adults and Adolescents > 12 years: 2 sprays in each nostril once daily (each spray = 50mcg of Momethasone in each spray , totally daily dose of 200 mcg) for a period of one month

OR

- **Flucatisone propionate,** Children 6 - 11 years: The recommended starting dose is one to two spray actuation (27.5 micrograms of fluticasone furoate per spray actuation) in each nostril once daily (total daily dose, 55 micrograms). Patients not adequately responding to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) may use two spray actuations in each nostril once daily.

Adults and Adolescents > 12 years: The recommended starting dose is two spray actuations (27.5 micrograms of fluticasone furoate per spray actuation) in each nostril once daily (total daily dose, 110 micrograms).

Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril (total daily dose 55 micrograms) may be effective for maintenance.

C/Is: Should be avoided in children under 6 years.

N.B: choice of treatment should be based on the type of allergic rhinitis and the severity of symptoms.

EPISTAXIS

BRIEF DESCRIPTION

- Epistaxis, bleeding from the nose, is a common complaint. It is rarely life threatening. It can be classified as mild, recurrent or sever/persistent. It can also be classified based on the cause as local and systemic. The local causes can be classified as anterior and posterior. 90% of the local case is anterior.

RISK FACTORS FOR EPISTAXIS

- Digital manipulation of the nose
- Drug abusing (nasal sniffers)
- Acute rhinitis (common cold)
- Excessive use of nasal spray
- Smoking can cause nasal dryness

CLINICAL FEATURES

Symptom

- Anterior nasal bleeding or posterior nasal bleeding from the throat
- If the bleeding is severe it can cause shock

Sign

- Look for signs of bleeding in the anterior nasal septum
- Look for signs of systemic bleeding like gingival bleeding, joint bleeding, petechia rash, subconjunctival hemorrhage
- Blood vomiting in the case sever posterior nasal bleeding due to swallowing

Investigations

- If you suspect systemic cause look for: CBC, coagulation profile, liver function test,

TREATMENT

Objective

- Stop epistaxis
- Replace blood if bleeding is severe
- Prevent recurrence of epistaxis

MANAGMENT

For sever persistent epistaxis

1. Resucitation
2. Stop/localize the bleeding
3. Pinching the anterior aspect of the nose for 15 minutes.
4. Cold compression over the major neck vessels
5. Position the head forward (Tilt forward)
6. If not responding, apply cautery (silver nitrate (Silver Nitrate + Potassium Nitrate, apply to mucous membranes and other moist skin surfaces only on area to be treated 2-3 times/week for 2-3 weeks) or electronic cautery),
7. If not responding to cautery applies anterior nasal packing. The anterior nasal packing can be Vaseline gauze application or merocele.
8. If the anterior nasal packing is not working, the posterior nasal packing can be applied. The posterior nasal packing can be inflation of balloon or folly catheter.
9. If no response with this measure, refer for surgery. N.B. When conservative measures fail to stop the bleeding, embolization or surgical ligation of the offending vessels is needed.

First line

- The role of oral antibiotic can be given for anterior and posterior nasal packing lasting longer than 48 hours for the prevention of toxic shock syndrome among immunocompromised hosts, diabetes mellitus, and advanced age.

- **Amoxicillin,** children; 125mg/5ml – 250mg/5ml P.O., TID 7 – 10 days adults; 250 – 500mg. caps P.O., TID 7 – 10 days

Alternatives

- **Amoxicillin/Clavulanate**, children;156mg/5ml P.O., TID or 312mg/5ml P.O. TID 7-10 days; adults; 375mg P.O., TID for 7-10 days or 625mg P.O., BID for 7-10 days

Foreign bodies in the nose

- These are usually found in children in the 2 – 3 year age group. Usually the insertion is done while playing by themselves, when left alone.

CLINICAL FEATURES

- These include unilateral nasal obstruction
- Worsening chronic purulent rhinitis or sinusitis
- Unilateral fetid secretion and formation of rhinolith due to deposition of calcium around the foreign body.

INVESTIGATIONS

- Anterior rhinoscopy
- X-ray if you suspect radiopic foreign body

TREATMENT

Objective

- Remove the foreign body
- Prevent complications

Non pharmacologic

- Remove the foreign body.

Nasal bone fracture

- Most common facial fracture
- Third most fractured bone next to wrist & clavicle
- High index of suspicion for fracture

CLINICAL FEATURE

- Change in appearance
- Epistaxis, Nasal obstruction
- Instability, Mobility, Crepitation Lacerations, Septal hematoma

INVESTIGATION

- Nasal X-rays, variable, reliability
- Early ENT referral (<5 days) needs for displaced fracture and open fracture

MANAGEMENT:

- Closed/ Open reduction (early)
- Septorhinoplasty (late)

COMPLICATION:

- Septal hematoma
- Nasal obstruction

20.3 THROAT CONDITIONS

ACUTE TONSILLITIS

BRIEF DESCRIPTION

- Acute infection of the lymphoepithelial tissue of the faucial isthmus, the palatine tonsil, and pharyngeal (adenoid) tonsil, lingual and tubal tonsil is known as tonsillitis.

- The commonest causes are viral, followed by less likely beta-Streptococci, Staphylococci, Streptococcus Pneumoniae (Diplococcus pneumoniae) and Haemophilus.

CLINICAL FEATURES

Symptoms

- Low/High Fever and possibly chills, especially in children.
- Persistent pain in the oropharynx or Naso pharynx
- Pain on swallowing that radiates to the ear.
- Opening the mouth is often difficult and painful if it is complicated.
- Usually associated with systemic symptoms like Headache and marked feeling of malaise, chills, and rigor.

Signs

- Inflamed and reddened enlarged tonsils
- Exudates are apparent in bacterial tonsillitis
- Tender cervical lymphadenopathy

INVESTIGATIONS

- CBC and ESR
- Culture from throat swab.

TREATMENT

Objective

- Treat infection
- Shorten the duration of the disease
- Prevent complication
- Relieve pain

Non pharmacologic

- Gargling with warm Normal saline solution

Pharmacologic

- The management is conservative
- The indication for bacterial tonsillitis, high grade fever, exudative tonsillitis, and tender cervical lymphadenopathy. Several symptoms that are not suggestive of group A Streptococcus are cough, conjunctivitis, and coryza.

First line

- **Amoxicillin** 250-500mg P.O., TID for 7 – 10 days. 125mg/5ml, 250mg/5ml P.O., TID for 7 –10 days. (pedi; 50 mg/kg PO once daily to a maximum of 1000-1200 mg x 10 days)

Alternatives

- Consider cephalosporin (e.g. **Cephalexin** 500 mg po bid x 10 days)

OR

- If there is poor response go for **Amxoicillin – Clavulanate:** pediatric dose: 45 mg/kg/day in two divided doses for ten days (Adult dose: 875/125 mg PO bid x 10 days)

FEVER MANAGEMENT

- **Paracetamoll**, 500mg P.O, PRN.

Local complications

- peritonsillar abscess (the complications may also include, paraphayrengial abscess and retropharyngeal abscess, not addressed here)
- In adiaguatly treated acute or chronic tonsillitis can spreed to the surrounding tissue and form abscess called peritonsillar abscess

CLINICAL FEATURES OF PERITONSILLAR ABSCESS

- Severe pain such that the patient often refuses to eat
- The head is held over to the diseased side, and rapid head movements are avoided.

- The patient has sialorrhea and oral fetor
- Swelling of the regional lymph nodes,
- Fever with high temperatures of 39°C to 40°C and the general condition deteriorates rapidly.
- Redness, and protrusion of the tonsil, the faucial arch, the palate and the uvula
- Marked tenderness of the tonsillar area

TREATMENT OF PERITONSILLAR ABSCESS

- Early referral for drainage of the absccess and tosnillectomy

Systemic complication

- Septicemia
- Rheumatic heart disease
- Post streptococcal plomerulonephritis

ADENOID TONSILLAR HYPERTROPHY

BRIEF DESCRIPTION

- Enlargement of the adenoids with or without concomitant palatine tonsillar enlargement.
- Leads to obstructive symptoms in children peaking at ages 4-5, and is rare after the age of 12.

CLINICAL FEATURES

Symptoms

- Nasal obstruction, snoring
- Recurrent rhino sinusitis or otitis media
- Nasal discharge, post nasal drip and cough

- Obstructive sleep apnea characterized but loud snoring at night, recurrent apneic episodes enuresis, and day time solomonence, poor school performance, cognitive impairment

Signs

- Adenoid Facies (Open mouth, high arching palate, narrow mid face, malocclusion)
- Hypo nasal voice
- Bilateral palatial tonsillar enlargement

INVESTIGATION AND DIAGNOSIS

- Diagnosis can be made through direct visualization of the adenoids via flexible nasopharyngoscope or mirrors (Posterior Rhinoscopy)
- Lateral Neck X-RAY can show the adenoid shadows

TREATMENT

- Referral of children to ENT care centers is mandated, if the child has symptoms of obstructive sleep apnea or recurrent tonsillitis. Recurrent tonsillitis is defined as an acute attack of tonsillitis 7 times in a year or five times a year for two consecutive years or three times per year for their consecutive years.
- Indication for referral of adeno tonsillar hypertrophy for surgical management
- obstructive sleep apnea
- Recurrent tonsillitis
- Failure to thrive
- Recurrent peritonsillar absence
- Malignancy suspicion
- If the patient has severe dysphagia

ACUTE LARYNGITIS

BRIEF DESCRIPTION

- This is an inflammation strictly localized to the vocal cords, usually of viral origin. Acute laryngitis is usually due to ascending or descending infection from the other parts of the airway. In children there is a danger of airway obstruction.

CLINICAL FEATURES

- Hoarseness of the voice
- Aphonia
- Pain in the larynx and coughing attacks
- In children there is a danger of airway obstruction

Investigations

- Laryngoscopy shows red and swollen vocal cords lose their normal color

Treatment

Objective

- Relieve airway obstruction

Non pharmacologic:

- Voice hygiene (voice rest, rehydration)
- Mist therapy (application of steam or inhalant)

PHARMACOLOGIC

First line

- Antibiotics are not usually recommended due to the viral onset of the disease If there is an upper airway obstruction
- **Prednisolone**, 40-60mg P.O., daily based on severity, the dose is reduced by 5mg every 5 days. NB: Glucocorticoids should only be given if there is concern for airway compromise.

FOREIGN BODY IN THE THROAT

- All pharyngeal foreign bodies are medical emergencies that require airway protection.

CLINICAL FEATURES

Symptoms

- History of chocking,
- Dysphagia and odynophagia
- Dysphonia and hoarseness
- Coughing and stridor

INVESTIGATION AND DIAGNOSIS

- High degree of suspicion is required especially in children with partial obstruction
- Neck and Chest X-RAY for radiopaque objects.

GOAL OF TREATMENT

- Secure airway

N.B. Refer patients for immediate endoscopic removal

20.4 SALIVARY GLAND CONDITIONS

MUMPS (EPIDEMIC PAROTITIS)

- Mumps is a disease characterized by swelling of one or more salivary glands.
- The parotid glands are the salivary glands most commonly involved with mumps,
- In 75-80% of cases both glands are involved.

CLINICAL FEATURES

Symptoms

- Ear pain localized to the ear lobe aggravated by chewing
- Swelling at the angle of the jaw
- Sour taste in the mouth
- Fever (usual subsides within 7 days)
- Rarely sudden hearing loss can occur
- In adult males orchitis (testicular swellings can occur occasionally)

Signs

- Tender swelling of the parotids or other salivary glands
- Erythematous and edematous submandibular duct or stepsons (parotid duct)

INVESTIGATIONS

- Diagnosis is clinical

TREATMENT

Objective

- Relieve symptoms

Non pharmacologic:

- Massage the gland

Pharmacologic

First line

- **Paracetamol**, children; 30-40mg/kg/24 hr. divided into 4 – 6 doses adults; 1000mg P.O, every 6 hrs PRN

Alternatives

- **Tramadol**, 100 mg P.O., every 6 hrsPRN for adults.

N.B. Not recommended for chidren below 12 years of age

Acute and non-chronic non-obstructive suppurative Sialadenitis

- Acute bacterial infection of the salivary glands usually involves the paratoid glands. This condition is usually seen in debilitated patients. The usual causative organism is Staphylcoccus aureus.

CLINICAL FEATURES

- Pain and swelling of the involved gland
- Purulent secretions can be expressed from the orifice of the duct
- Fever

INVESTIGATIONS

- Solography shows a tree in leaf appearance
- Tissue should be taken for histology in doubtful cases

TREATMENT

Objective

- Control pain
- Prevent recurring episodes

Non pharmacologic

- Bed rest
- Restricted jaw movement

Pharmacologic

First line

- **Cloxacillin**, 500mg P.O., QID for 7 – 10 days. 50 – 100mg /kg/24hrs. P.O., divided into 4 doses for 7 - 10 days.

Alternatives

- **Cephalexin**, children; 6 to 12 mg/kg PO Q 6 hours. Maximum 25mg/kg Q

6 hours adults; 50mg to 1gm QID PO Q6 hours

- **If penicillin allergy, Clindamycin**, 150 to 450mg P.O., QID or 300mg IM or IV QID or TID. In severe infections 20mg/kg/24hr. IM or IV into 4 doses.

20.5 UPPER AIRWAY OBSTRUCTION

- It is difficulty of breathing caused by obstruction occurred above the thoracic airway (which could be nasopharynx, oropharynx, laryngeal or extra-thoracic tracheal airway)
- Caused by obstructive mass or post inflammatory

CLINICAL FEATURES

- Hoarseness of voice, hypo nasal or pharyngeal (hot potato speech) based on location of obstruction.
- stridor (inspiratory, expiratory or biphasic) based on site obstruction.
- tachypnea, tachycardia.
- Cyanosis & loss of consciousness are late signs.

MANAGEMENT

- Try to calm the patient & keep breathing (avoid crying in pediatric age & talk in adults.
- Administration of intranasal or face mask oxygen.
- Administration of adrenaline inhalation (nebulization) & steroid if we suspect post-inflammatory obstruction.
- Secure the airway: non-surgical (intubation) or surgical (cricothyrotomy and tracheotomy).

CHAPTER 21:

ORALFACIAL AND DENTAL CONDITIONS

21.1 PERIODONTAL CONDITIONS

21.1.1 GINGIVITIS

BRIEF DESCRIPTIONS

- Gingivitis refers to inflammation of the gum.
- Dental plaque-induced gingival disease is the most common form of gingivitis.
- Dental plaque, also known as bacterial biofilm, is a dense mass of bacterial colonies living in matrix that forms around the gingival margin (gum line.
- Chronic gingivitis results from the inflammatory response to the accumulation of dental plaque next in the gingival margin.
- Infectious pathogens (mixed anaerobic and aerobic oral flora, e.g. *Streptococcus viridians*, facultative *streptococci*; fusiform bacteria, spirochetes, viruses, fungi), poor oral hygiene with plaque accumulation or chemicals are the major causes for chronic gingivitis.

CLINICAL FEATURES

- Gingival redness and swelling
- change in the normal gum contour
- Sometimes it may be painful
- Watery exudate or bleeding,
- Gum recession

DIAGNOSIS

- The diagnosis is made based on clinical evaluation

TREATMENT

Objective

- Relieve pain
- Improve bad oral breath
- Remove plaque accumulation

Non-pharmacologic

- Oral hygiene
    - Oral hygiene after each meal to remove plaque and food debris.
    - Frequent thorough brushing of teeth, at least twice daily.
    - Dental flossing daily
    - Homemade warm saline rinse
    - Dissolve 1/2 teaspoon of table salt (sodium chloride) in 200 ml warm water. Rinse mouth for one minute twice daily but do not swallow.
- Polishing: to remove plaque and calculus deposits

Pharmacologic

1. ORAL ANTISEPTICS

- Chlorhexidine 0.2%, 15 mL as a mouthwash, 2–4 times daily for 5 days use after brushing and flossing.
- Hydrogen peroxide solution 3%, 3-4 times daily

OR

- Povidone iodine 0.5% used 3-4 times daily

2. SUPPORTIVE TREATMENT

- Pain management

- Paracetamol, oral, 1000mg (child: 15mg/kg/day), 6 hourly when required to a maximum of 4 doses per 24 hours

OR

- NASIADS e.g. Ibuprofen 400mg Ibuprofen 400 mg every 8 hours (Child: 7-13 mg/kg every 8 hours)

3. ANTIBIOTICS

- Antibiotics are not routinely indicated.
- Only if systemic signs or symptoms present e.g. fever
  - Amoxicillin oral 500 mg every 8 hours for five days (Child: 25 mg/kg every 8 hours) 5- 7 days

    PLUS

  - Metronidazole oral 250- 500 mg every 8 hours (Child: 10-12.5 mg/kg every 8 hours) 15 mg/kg 12 hourly for 5 -7days
  - For penicillin allergic patients: Doxycline 100mg PO BID X 5-7 days or Clindamcycin 300 -450 PO TID x 5-7 days
  - Doxycycline is contraindicated in pregnant, lactating mothers and children less than 12 years.

REFERRAL

- Refer to a dentist for scaling, polishing, to removal of plaque and calculus.

FURTHER READING

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21.1.2 PERIODONTITIS

BRIEF DESCRIPTION

- Periodontitis occurs when inflammation or infection of the gums (gingivitis) is not treated. The infection and inflammation spreads from the gums (gingiva) to the ligaments and bone that support the teeth.
- It is characterized by teeth losing support, becoming loose in their socket, and eventually fall out.
- Mixed bacterial microbial flora commonly, B. gingivitis, B. forsythus, B. intermedius, Wolinella sp., and Fusobacter, are major causes.

CLINICAL FEATURES

- Bleeding of gums on probing and brushing
- Foul smelling breath
- Tooth sensitivity to heat changes
- Presence calculus below the gum
- Increased tooth mobility

INVESTIGATIONS AND DIAGNOSIS

- If periodontitis is clinically suspected, refer patients to a dentist
- Periodontal probing
- Intra oral x-ray

TREATMENT

Non-pharmacologic treatment

- Provide advice oral hygiene (see section on gingivitis)

PHARMACOLOGIC TREATMENT

- Chlorhexidine 0.2%, 15 mL as a mouthwash, 2–4 times daily for 5 days use after brushing and flossing.

OR

- Hydrogen peroxide solution 3%, 3-4 times daily

OR

- Povidone iodine 0.5% used 3-4 times daily

REFERRAL

- Refer all patients with periodontitis to a dental specialist for possible scaling, root planning, and polishing, to remove plaque and calculus deposits.

FURTHER READING

1. F. Kinane1, P. G. Stathopoulou1 and P. N. Papapanou. Periodontal diseases. Nature Reviews Disease Primers. 2017; Volume 3, Article Number 17038. doi:10.1038/nrdp.2017.38. www.nature.com/nrdp

2. Prevention and Treatment of Periodontal Diseases in Primary Care. 2014 Scottish Dental Clinical Effectiveness Programme. NHS Scotland. www.sdcep.org.uk

3. S. Murakami. B. L. Mealey, A. Mariotti, I. L.C. Chapple. Dental plaque–induced gingival conditions. J Clin Periodontol. 2018;45(Suppl 20):S17–S27. DOI: 10.1111/jcpe.12937

21.1.3 NECROTIZING ULCERATIVE GINGIVITIS (NUG) AND NECROTIZING ULCERATIVE PERIODONTITIS (NUP)

BRIEF DESCRIPTION

- It is also named as Vincent's gingivitis, trench mouth, acute ulcerative gingivitis, necrotizing gingivitis
- Necrotizing ulcerative gingivitis is a painful ulceration of the papillae between the teeth with grey necrotic tissue visible on the surface of the ulcers.
- It is characteristically a rapid onset disease with typical clinical features.

- It mainly affects patients with HIV infection and low CD, other patients with severe immunosuppression resulting from cancer, severe malnutrition, poorly controlled diabetes, and smokers.
- If NUG is not treated early it might lead to destruction not only the periodontal structures (NUP) but also the buccal mucosa.
- Typical microorganisms: fusiform bacteria, Prevotella intermedia, Porphyromonas gingivalis, Treponema species, and Candida albicans.

CLINICAL FEATURES

Symptoms

- NUG is characterized by acute onset of symptoms
- Intense pain
- Swelling and redness of the gingival margins
- Bleeding of the gum
- Difficulty drinking and eating

Signs

- Necrosis of gingival tissues
- Yellowish-white ulceration of the gingival
- Bleeding on minimal or no provocation
- Loss of periodontal ligament and alveolar bone
- The ulcerated areas are separated by linear erythematous tissue
- Severe loss of periodontal attachment
- The bone can occasionally be exposed,
- Lymphadenopathy

DIAGNOSIS AND INVESTIGATIONS

- The diagnosis of NUG is made clinically based on the presence of typical clinical features in individuals with risk factors.

- The most important features needed for the diagnosis are acute onset pain, necrosis, and bleeding.

TREATMENT

Non-pharmacologic

- Rinse mouth with mouthwash 3 times a day: warm salt solution (1/2 a teaspoonful of salt in 200ml warm water)
- Debridement of necrotic tissue
- Management of underlying condition
- Advise on nutrition, decreasing stress, and to quit smoking.

Pharmacologic

1. **ORAL ANTISEPTICS**

- Hydrogen peroxide solution 6%, (add 15 ml to a 200 ml warm water)

OR

- Chlorhexidine solution 0.2% , 15 ml as a mouthwash, 3–4 times daily after brushing and flossing

OR

- Povidone iodine 0.5%, use 3-4 times daily

2. **PAIN MANAGEMENT**

- Paracetamol, oral, 1000mg (child: 15mg/kg/day), 6 hourly when required to a maximum of 4 doses per 24 hours

OR

- Non-steroidal anti-inflammatory drugs e.g., Ibuprofen 400mg Ibuprofen 400 mg every 8 hours (Child: 7-13 mg/kg every 8 hours for three days)

OR

- Diclofenac 50mg PO every 8 hours for three days

3. **ANTIBIOTICS**

- **Amoxicillin/Clavulinic acid PO 625mg** every 8 hour 5-7 days (Children: 25 mg/kg/dose of the amoxicillin component 8 hourly)

  OR

- **Amoxicillin 500mg** PO every 8 hours (Child: 25 mg/kg every 8 hours) PLUS **Metronidazole 500mg** PO every 8 hours (child: 10-12.5mg/kg every 8 hours) 5- 7 days
- For patients who cannot tolerate oral antibiotics
  - **Ceftriaxone 1-2gm**, IV/every 24 hour PLUS Metronidazole 500mg, IV 8hourly.
- For penicillin allergic patients : Doxycline 100mg PO BID X 5-7 days or Clindamcycin 300-450 PO TID x 5-7 days
  - **Ddoxycycline** is contraindicated in pregnant, lactating mothers and children less than 12 years.

REFERRAL

- Patients with NUG should be referred to dental specialist after appropriate supportive and antibiotics are given.

FURTHER READING

1. R. Malek, A. Gharibi, N. Khlil, and J. Kissa. Necrotizing Ulcerative Gingivitis. Contemp Clin Dent. 2017 Jul-Sep; 8(3): 496–500. doi: 10.4103/ccd.ccd_1181_16
2. E-Y Kwon, Y-K Choi , J. Choi , J-Y Lee et al. Effective Management of Acute Necrotizing Ulcerative Gingivitis with Proper Diagnosis and Immediate Treatment. J Korean Dent Sci. 2016;9(2):81-89 https://doi.org/10.5856/JKDS.2016.9.2.81

21.1.4 DENTAL CARIES

BRIEF DESCRIPTION

- Dental caries is a chronic non-communicable disease that affects people of all age groups worldwide.
- It is caused by an acid environment which results from the metabolism of carbohydrates/sugars by bacteria.
- The acidic environment enhances the growth acid-tolerant as well as acid-producing microorganisms.
- An acidic environment results in demineralization (loss of minerals) of the teeth.
- The lesion in dental caries could be non-cavitating or cavitating.
- Three types of caries depending on site of cavities— smooth surface, pit and fissure, or root caries.

CLINICAL FEATURES

Symptoms

- Usually asymptomatic in early stages
- Sensitivity to cold or hot
- Pain/toothache: initially in response to cold/hot/sweet drinks or foods but as the disease advances it may spontaneously

Signs

- Chalky white/black/brown spots on the chewing surface of the tooth
- Cavities on the tooth surface
- Tenderness on percussion
- Swelling at the base of the tooth
- The susceptible sites are areas of plaque accumulation which might not be accessible to cleansing e.g. pits and fissures

INVESTIGATION AND DIAGNOSIS

- The diagnosis of dental caries and assessing it severity are made based on the clinical features mentioned above.
- X-ray: Periapical x-ray may need to know the extent and treatment decision.

TREATMENT

Objectives

- Provide relief from pain
- Reminiralization and reduce demineralization of hard tissue
- Preserve the tooth without extraction
- Prevent infectious complication of the periodontal tissue including the jaw

Non-pharmacological treatment

1. Regular checkups to identify early cavities and other dental conditions
2. Filling and restoration with suitable materials

- **Non cavitating lesions**: A dentist needs to prioritize using either of the following
  - 1.23% APF (Acidulated phosphate) gel

    OR

  - 5% NaF (Sodium fluoride.) varnish every 3-6 months.
- **Cavitating lesions**: A dentist needs to prioritize either of the following options depending on the severity of the disease
  - Professional fluoride treatments (liquid, gel, foam or varnish) : for early stages
  - Fillings (restoration): when decay has progressed beyond the early stages
  - Crowns (a custom-fitted covering that replaces the natural crown): for extensive decay or weakened teeth

- o Root canals: when decay reaches the inner material of tooth (pulp),
- o Tooth extractions: for severely decayed tooth that they can't be restored and must be removed.

PHARMACOLOGIC TREATMENT

- Pain management: for toothache (see pain management in periodontal diseases)

PREVENTION

- Maintenance of good oral hygiene: Cleaning teeth using fluoride based toothpaste at least twice per day
- Reduce intake of sweet/sugary foods or drinks
- Encourage mouth rinses
- Sealant application in children: Sealants are materials that seal pits and fissures on the surfaces of teeth and can prevent caries lesions
- Dental check up

REFERRAL

- Patients with dental caries need to be referred to a dentist (restorative or endodontic specialist) after pain management and advice or oral hygiene is given.

FURTHER READING

1. N. B. Pitts, D. T. Zero, P. D. Marsh, K. Ekstrand et al. Dental caries. Nature Reviews Disease Primers 2017 Volume 3 | Article Number 17030. http://dx.doi.org/10.1038/nrdp.2017.30
2. Mark B. Stephens, Joseph P. Wiedemer, George M. Kushner. Dental Problems in Primary Care. Am Fam Physician. 2018;98(11):654-660.
3. R. L. Slayton; O. Urquhart; M.W.B. Araujo; M. Fontana et al. Evidence-based clinical practice guideline on nonrestrictive treatments for carious lesions: A report from the American Dental Association. JADA 2018:149(10):837-849 https://doi.org/10.1016/j.adaj.2018.07.002

21.2 ODONTOGENIC AND NON-ODONTOGENIC OROFACIAL INFECTIONS

21.2.1 PERIAPICAL ABSCESS

BRIEF DESCRIPTION

- A dental abscess is a localized collection of pus in the structures surrounding with a tooth.
- The major forms of dental abscess are **periapical abscess and periodontal abscess.**
- In a periapical abscess the location of the abscess is at tip (apex) of the root of the tooth and in periodontal abscess the location is alongside a tooth, within the tissue supporting the side of the tooth.
- Differentiating periapical abscess from periodontal abscess is important as the management is different.
- Periapical abscess is a consequence of dental pulp inflammation/infection (pulpitis) caused by dental caries or trauma.
- Left untreated a root abscess may extend it to soft tissue or the bone causing cellulitis or osteomyelitis respectively.

CLINICAL FEATURES

Symptoms

- Severe pain that disturb sleep and difficult to locate the culprit tooth
- Pain causing difficulty in occlusion(chewing)
- Swelling around gum and/or face
- Discharge
- Fever if the infection has spread

Signs

- Tenderness of vertical percussion
- Swelling around the root area of the affected tooth

Table 21.1: Differentiating apical abscess from periodontal abscess

Differentiating apical abscess from periodontal abscess		
Clinical feature	**Periapical abscess**	**Periodontal abscess**
Pain characteristics	Severe, deep, throbbing	Dull and less severe
Localizing the pain	Patient usually unable to locate the offending tooth	Patient can usually locate the offending tooth e
Tenderness	More severe on vertical percussion	More severe on lateral percussion
Area of swelling	Apex	Gingival margin

INVESTIGATION AND DIAGNOSIS

- X-ray is indicated to assess the possible bone involvement
- CBC and CRP/ESR: if there are
- Diagnosis is mainly based on clinical evaluation

TREATMENT

Non-pharmacologic treatment

- Root canal treatment
- Trephination:
  - A procedure in which the alveolar cortical plate is surgically perforated in order to release accumulated exudate(pus).
  - A minor vertical incision is made next to the tooth, and the mucosa is pulled back.
- Excision and drainage

- Tooth extraction: to be done if the other options are not possible.

PHARMACOLOGIC TREATMENT

1. **Pain management:** see section on periodontal conditions
2. **Antibiotics**

- Indicated in patients having systemic symptoms like fever or having regional lymphadenopathy or bone involvement.
- If indicated the following are the antibiotics of choice based on patient oral intake ability.
  - o **Amoxicillin/Clavulinic acid** PO 625mg every 8 hour 5-7 days (Children: 25 mg/kg/dose of the Amoxicillin component 8 hourly)

    OR

  - o **Amoxicillin 500mg** PO every 8 hours (Child: 25 mg/kg every 8 hours) PLUS **Metronidazole 500mg** PO every 8 hours (child: 10-12.5mg/kg every 8 hours) 5- 7 days
  - o For patients who cannot tolerate oral antibiotics
- Ceftriaxone 1-2gm, IV/every 24 hour PLUS Metronidazole 500mg, IV 8hourly.

  OR

- Ampicillin 1000mg, IV, every 6 hourly (Child: 100-150mg/kg/day divided in to 4 to six doses) PLUS Metronidazole 500mg, IV 8hourly (Child: 10-12.5mg/kg every 8 hours)
  - o **For penicillin allergic patients**
- **Doxycline 100mg** PO BID X 5-7 days or Clindamcycin 300-450 PO TID x 5-7 days
  - o For patients who are allergic to penicillin and can't tolerate oral intake
- **Clindamycin 600mg,** IV, every 8 hours (Child 30 to 40mg/kg/day divided in to 3 to 4 doses)

REFERRAL

- All patients with periapical abscess need to be seen by a dentist. If there is no dental service in the health facility, the patient should be referred without undue delay.

FURTHER READING

1. Management of Acute Dental Problems Guidance for healthcare professionals. 2013 Scottish Dental Clinical Effectiveness Programme. NHS Scotland. www.sdcep.org.uk

2. Justin L. Sanders; Richard C. Houck. Dental Abscess. Stat Pearls [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK493149/

3. Mark B. Stephens, Joseph P. Wiedemer, George M. Kushner. Dental Problems in Primary Care. Am Fam Physician. 2018;98(11):654-660.

21.2.2 PERIODONTAL ABSCESS

BRIEF DESCRIPTION

- A periodontal abscess is a localized abscess infection within the tissues adjacent to the periodontal_pocket.
- It that can lead destruction of the periodontal ligament and bone.
- It is caused by entry of virulent organisms in to an existing pocket or a foreign body in a healthy periodontal area.
- Differentiating periodontal abscess from periapical abscess is important as the management is different.

CLINICAL FEATURES

Symptoms

- Pain around the culprit area
- Swelling of the gum and the surrounding tissue

- Difficulty of opening the mouth (trisumus).

Signs

- A smooth, shiny, tender swelling of the gingiva
- Pus discharge around the gingiva of affected tooth/teeth
- Tenderness of lateral percussion
- Bleeding and/or pus discharge on probing
- Regional lymph node enlargement

INVESTIGATION AND DIAGNOSIS

- Diagnosis is made mainly on clinical grounds: through careful medical, dental history and examination.

TREATMENT

Objectives

- Immediate relief of pain
- Preventing local or systemic spread of infection
- Draining the abscess and debridement

Non-pharmacologic treatment

- The main stay of treatment for periodontal abscess is incision & drainage along with debridement.

Pharmacologic treatment

1. **Antibiotics:**

- Antibiotics are only indicated in patients having systemic symptoms like fever or there is a regional lymphadenopathy
- If indicated the following are the antibiotics of choice based on patient oral intake ability.
    - **Amoxicillin/Clavulinic** acid PO 625mg every 8 hour 5-7 days (Children: 25 mg/kg/dose of the **Amoxicillin** component 8 hourly)

OR

- o **Amoxicillin 500mg** PO every 8 hours (Child: 25 mg/kg every 8 hours) PLUS **Metronidazole 500mg** PO every 8 hours (child: 10-12.5mg/kg every 8 hours) 5- 7 days
- o For patients who cannot tolerate oral antibiotics

- **Ceftriaxone 1-2gm,** IV/every 24 hour PLUS Metronidazole 500mg, IV 8hourly.

OR

- **Ampicillin 1000mg**, IV, every 6 hourly (Child: 100-150mg/kg/day divided in to 4 to six doses) PLUS Metronidazole 500mg, IV 8hourly (Child: 10-12.5mg/kg every 8 hours)
  - o For penicillin allergic patients
- **Doxycline 100mg** PO BID X 5-7 days or Clindamcycin 300-450 PO TID x 5-7 days
  - o For patients who are allergic to penicillin and can't tolerate oral intake
- **Clindamycin 600mg,** IV, every 8 hours (Child 30 to 40mg/kg/day divided in to 3 to 4 doses)

REFERRAL

- All patients with periodontal abscess need drainage of the abscess by a dental specialist/dentist.
- Delaying referral by giving antibiotics is a malpractice and should be avoided.

FURTHER READING

1. Management of Acute Dental Problems Guidance for healthcare professionals. 2013 Scottish Dental Clinical Effectiveness Programme. NHS Scotland. www.sdcep.org.uk
2. Yasamin Yousefi; Jane Meldrum; Abdul H. Jan. Periodontal Abscess. Stat Pearls [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK560625/

3. Ignacio Christian Marquez. How Do I Manage a Patient with Periodontal Abscess? *Can Dent Assoc 2013;79:d8*

21.2.3 PERICORONITIS

BRIEF DESCRIPTION

- Pericoronitis is inflammation of the soft tissues covering the crown of erupting tooth.
- It commonly occurs with the eruption of in association mandibular third molar (wisdom) teeth.
- Impaction of food and plaque under the gingiva flap provide a medium for bacterial multiplication. Biting on the gum flap by opposing tooth causes laceration of the flap, increasing the risk of infection and associated swelling.
- Involved bacteria are similar to those causing gingivitis and periodontitis.

CLINICAL FEATURES

Symptoms

- High temperature,
- Severe malaise
- Discomfort during swallowing and chewing

Signs

- Well localized dull pain, swollen and tender gum flap
- Signs of partial tooth eruption or interruption in the region
- Pus discharge beneath the flap may or may not be observed
- Foetor-ox oris bad smell
- Trisumus
- Regional lymph nodes enlargement and tender

INVESTIGATION AND DIAGNOSIS

- Diagnosis is made mainly on clinical grounds: through careful medical, dental history and examination.
- Intra-oral x-ray

TREATMENT

Objectives

- Debridement of the occluded area of impacted tooth and soft tissue
- Pain relief
- Prevention of spread of infection

Non-pharmacologic

- The preferred management is conservative
  - Oral hygiene
  - Antiseptic mouthwash: see periodontal disease
  - pain management
- If the patient presents with one or more of the following further intervention is needed
  - Swollen face
  - Lymphadenopathy
  - Trisumus
  - Difficult of swallowing
  - Signs of systemic infection
  - Airway obstruction
- Interventions that can be done
  - Excision of the operculum/flap (flapectomy)
  - Extraction

- Others: Grinding or extraction of the opposing tooth

PHARMACOLOGIC

1. Pain management : see section on periodontal diseases
2. Antibiotics

- Indications for antibiotics: the presence of either of the following warrants
  - Fever
  - Painful mouth opening
  - Difficulty of opening the mouth(trisumus)
  - Swelling
  - Lymphadenopathy and fever.
- Antibiotic choice: similar to periapical or periodontal abscess(see pharmacologic treatment of these conditions)

FURTHER READING

1. Tara Renton and Nairn H F Wilson. Problems with erupting wisdom teeth: signs, symptoms, and management. Br J Gen Pract 2016;DOI: 10.3399/bjgp16X686509.
2. Management of Acute Dental Problems Guidance for healthcare professionals. 2013 Scottish Dental Clinical Effectiveness Programme. NHS Scotland. www.sdcep.org.uk
3. Mark B. Stephens, Joseph P. Wiedemer, George M. Kushner. Dental Problems in Primary Care. Am Fam Physician. 2018;98(11):654-660.

21.2.4 LUDWIG'S ANGINA

BRIEF DESCRIPTION

- Ludwig's angina is a rapidly evolving bilateral, diffuse cellulitis involving the sublingual, submandibular, and submental spaces.

- The infection usually starts from an infected 2nd or 3rd mandibular molar tooth.
- It spreads to the surrounding tissue rapidly and results in number fatal complications.
- Airway compromise, aspiration pneumonia, necrotizing fasciitis, extension in to the mediastinum or pleural cavity, carotid sheath and carotid artery involvement, thrombophlebitis of the internal jugular vein are some of the potential complications.
- Characteristically it does not form abscesses or cause lymphadenopathy.
- It is polymicrobial infection; streptococcus viridians and oral anaerobes are the most common organisms. In immunocompromised hosts gram negatives and staphylococcus aureus may also present.
- Ludwig's angina is a medical emergency; early recognition and treatment is crucial.

CLINICAL FEATURES

Symptoms

- Systemic symptoms: Fever, chills, and malaise
- Local symptoms: pain and swelling over the floor of the mouth, dysphagia, drooling
- Symptoms of airway compromise: muffled voice, difficult to speak and air hunger

Signs

- Swelling in the submandibular, submental and area: Tender, symmetric, indurated (wood like) swelling, no fluctuance.
- Sometimes crepitus is palpable in the swelling.
- The patient may lean forward to maximize airway space: a sign of impending airway obstruction
- The floor of the mouth is elevated and tender.

- Hoarseness
- Dysphonia ("hot potato voice")
- Stridor
- Cyanosis: an ominous sign of airway obstruction.
- Lymphadenopathy is not usually present.

Investigations and diagnosis

- The diagnosis of Ludwig's angina is made on clinical grounds.
- Imaging: CT scan may help in the diagnosis nut is not mandatory.

TREATMENT

Objectives of treatment

- Keep airway patent
- Control infection

Non-pharmacologic management

- **Airway management**
    - Airway management is the most crucial management
    - The patient airway status should be frequently assessed: voice quality, ability to speak
    - Stridor, respiratory distress and cyanosis are late signs
    - If the patient has signs of airway compromise the: tracheostomy or cricothyroidotomy are the preferred means.
    - Oral endotracheal intubation is generally difficult, traumatic and unsafe.
- **Surgery**
    - Surgical drainage is not usually necessary as drainable abscess is not common in the early stages

- If abscess is clinically suspected or confirmed by imaging surgical drainage is necessary.

PHARMACOLOGIC MANAGEMENT

- **Antibiotics**: broad spectrum antibiotics need to be initiated as early as possible
  - **Immunocompetent patients**
    - Penicillin G (2 to 4 MU IV every four to six hours) or Ampicillin 1gm IV every 6 hourly

      PLUS
    - Metronidazole (500 mg IV every eight hours)
  - **If Immunocompetent and penicillin allergic**
    - Clindamycin (600 mg IV every six to eight hours)
  - **Immunocompromised patients**
    - **Cefepime 2 g** IV BID

      PLUS
    - **Metronidazole** (500 mg IV every six to eight hours)

    Alternatives
    - **Meropenem** 18mg IV TID

      OR
    - **Piperacillin-tazobactam** (4.5 g IV every six hours)
  - **MRSA coverage**: in patients who are septic, hemodynamically unstable or rapidly deteriorating, add Vancomycin in addition to the above regimens (both Immunocompetent or immunocompromised)
    - **Vancomycin 15-20mg/kg/**dose, every 12 hours (maximum 2gm/dose)

- ○ **Duration of antibiotics**: 2-3 weeks, or until clear evidence of clinical resolution is present

REFERRAL

- Referral should only be done after making sure the airway is secured in patients with signs of airway compromise.
- If the patient does not have signs of airway compromise, the accepting hospital should be informed and the patient should be escorted by a health care professional.

FURTHER READING

1. M. Valléea, B. Gaboritb, J. Meyere, O. Malardf et al. Ludwig's angina: A diagnostic and surgical priority. International Journal of Infectious Diseases 93 (2020) 160–162. https://doi.org/10.1016/j.ijid.2020.01.028
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21.2.5 OSTEOMYELITIS OF THE JAW

BRIEF DESCRIPTION

- Osteomyelitis of the jaw is an infection of the jaw bones which starts from the outer layer and extends to inner bone.
- Once the infection becomes established, it ends up in the formation of pus. Pus collection in the medullary cavity of the bone results in decreased blood supply and ischemic necrosis of the area.
- It is more common in the mandibles.

CLINICAL FEATURES

Symptoms

- In the early stages patients, it might be asymptomatic or cause mild/vague pain over the jaw.

- Pain: variable severity
- Swelling over the jaw
- Difficulty of chewing
- Discharge: purulent in to the skin (sinus tract) or the mouth
- Systemic symptoms: fever and malaise

Signs

- Swelling
- Enlargement of regional lymph nodes
- Visible discharge from a skin (sinus tract) or oral cavity

INVESTIGATION AND DIAGNOSIS

- The diagnosis of osteomyelitis of the jaw might not always be straight forward.
- Clinical presentation, imaging and culture & sensitivity are important in establishing the diagnosis
- Culture and sensitivity from the discharge
- Culture and sensitivity from the discharge
- Imaging
- Conventional X-ray:
    - ○ For mandible: mandibular lateral oblique view or orthopantomograph
    - ○ For maxilla: water's view
    - ○ X-ray findings in early stages: periosteal bone reaction, widening of the mandible and an unidentifiable cortical-medullary border.
    - ○ X-ray finding in late stages: sequestera formation, sclerotic changes, and periosteal new bone formation.

TREATMENT

- **Objectives of treatment**
    - Removal of necrotic tissue to facilitate healing
    - Prevention of local and systemic spread of infection
    - Prevention of loss of functionality and disfigurement
- **Non-pharmacologic treatment**
    - Surgery: is needed for most patients with jaw osteomyelitis
    - Debridement of affected tissue, decortication, and sequestrectomy are standard surgical procedures.
    - Removal of involved teeth may be needed.
    - Early intervention reduces the morbidity and extent of the surgery required.
- **Pharmacologic treatment**
    - **Antibiotics:** Intravenous antibiotics for the at least the first 01 week after surgical debridement

1. **Initial empiric antibiotics**
    - **Ceftriaxone 1gm**, IV, every 12 hourly PLUS Metronidazole 500mg, IV every 8 hourly

    OR

    - **Clindamycin 600mg**, IV every 08 hourly
2. **Change antibiotics according to culture and sensitivity results**
3. **Changing to oral antibiotics:** After at least one week of IV antibiotics and surgical debridement
    - **Amoxicillin/Clavulinic acid PO 625mg** every 08 hour PLUS Metronidazole 500mg, PO, every 08 hour

    OR

- **Clindamycin 300-450mg**, PO, every 6hourly

Alternative

- **Amoxicillin 500mg,** PO, every 08 hour PLUS Metronidazole every 08 hour

4. **Duration of antibiotics:** At least six weeks

REFERRAL

- Patients with suspected or confirmed osteomyelitis of the jaw should be treated in a facility with expertise in performing the surgery of the jaw

FURTHER READING

1. Gudmundsson, T., Torkov, P., & Thygesen, T. (2017). Diagnosis and Treatment of Osteomyelitis of the Jaw – A Systematic Review (2002-2015) of the Literature. Journal of Dentistry & Oral Disorders, 3(4), [1066].

21.3 DENTINE HYPERSENSITIVITIES

BRIEF DESCRIPTION

- Dentine hypersensitivities (DHS) refer to the occurrence of pain derived from exposed dentin in response to chemical, thermal tactile or osmotic stimuli which cannot be explained as arising from any other dental defect or disease.
- Dentin is covered by enamel in the crown region and by cementum in the root region.
- When the cover of the dentin (enamel or cementum) is removed, it will be exposes, producing hypersensitivity.

CLINICAL FEATURES

- Sharp sudden onset and short lived pain
- Exposed root surface as a result of gingival (gum) recession may be seen

INVESTIGATION AND DIAGNOSIS

- Dentine hypersensitivity is a diagnosis of exclusion.
- All potential causes for pain should be excluded through careful history and physical examination.

TREATMENT

Objective

- Pain relief

Non pharmacological

- Proper oral hygiene instruction

Pharmacological

- Fluoride Gel application for dosage see under dental caries

FURTHER READING

1. N. Bubteina and S. Garoushi. Dentine Hypersensitivity: A Review. Dentistry 2015, 5:9. DOI: 10.4172/2161-1122.1000330.

2. Davari AR, Ataei E., Assarzadeh H. Dentin Hypersensitivity: Etiology, Diagnosis and Treatment; A Literature Review. J Dent Shiraz Univ Med Sci, Sept. 2013; 14(3): 136-145

3. Management of Acute Dental Problems Guidance for healthcare professionals. 2013 Scottish Dental Clinical Effectiveness Programme. NHS Scotland. www.sdcep.org.uk

21.4 POST TOOTH EXTRACTION COMPLICATIONS

21.4.1 POST EXTRACTION BLEEDING

BRIEF DESCRIPTION

- Bleeding from a socket can occur at any point in time after extraction.

- If it happens within the first 24 hours it called primary and if occurs after 24 hours it is called secondary.
- The commonest cause, eroding the clot due to repeated rinsing by the patient or inadequate compression.
- Bleeding diathesis, antiplatelet or anticoagulants, tooth or bony remnants are also important causes.

Clinical features

Symptoms

- Active bleeding from the socket

Signs

- The socket may or may not have blood clot
- Visible active bleeding site
- The socket may have remnants and damage of the bone.

INVESTIGATION AND DIAGNOSIS

The diagnosis of socket bleeding is clinical

- Investigations: Hemoglobin, blood-group and cross-match need to be done
- Platelet count, coagulation profile (PT/INR and aPTT)

TREATMENT

Objectives of treatment

- Restore hemodynamic status
- Arrest bleeding
- Prevent recurrence of bleeding

Non-Pharmacological Treatment

- Make sure airway is patent
- Assess for hemodynamically status (BP, postural drop in BP, tachycardia)

- Discontinue antiplatelet, anticoagulants
- Clear clot and examine the socket to identify source of bleeding
- Remove any foreign body and repack the socket with gauze
- Suturing may not be necessary, unless the gingiva is significantly traumatized.
- Cauterization: Chemical or electro cautery can be used if bleeding persists
- Give instructions for the patient

Do not dos:

- Rinse your mouth out today
- Drink alcohol or hot drinks today
- Smoke or use tobacco products for at least 24 hours
- Chew food for 4 hours, avoid hard foods for 24 hours
- Carry out any physical activity today (increasing blood pressure).

Do the following:

- Sip lukewarm drinks carefully
- Bite on gauze for 10 minutes if area bleeds, preferably sitting upright
- Rinse mouth gently with warm salt or Chlorhexidine (0.2%) after 24 hours.
- Clean teeth as normal, avoiding area of surgery for 24 hours

PHARMACOLOGIC TREATMENT

- Pain management: Avoid **NSAIDS, use Paracetamol or Tramadol**
- If bleeding persists: **Tranexamic acid 500 mg** every 8 hours
- If blood pressure is low: Transfuse with whole blood, until blood is available

give crystalloid (Normal saline or ringer's lactate)

REFERRAL

- If bleeding persists or bleeding diathesis is suspected, consult an internist or hematologist.
- Referral to a hospital where there is a hematologic service should only be done after exclusion of local causes and hemodynamic stabilization

FURTHER READING

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21.4.2 INFECTED SOCKET

BRIEF DESCRIPTION

- Infected socket is post extraction complication resulting from infection debris that is left under the mucoperiosteal flap and clot.
- It is one of the causes
- If not managed timely it may result in painful and if not managed well.

CLINICAL FEATURES

- Severe painful socket 2–4 days after tooth extraction
- Fever
- Necrotic blood clot in the socket
- Swollen gingiva around the socket

- Trisumus (inability to open the mouth) may be present

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of socket infection is based on clinical features.
- CBC, ESR or CRP might support diagnosis
- X-ray: is not routinely needed but if symptoms persist

TREATMENT

Objectives of treatment

- Controlling infection
- Preventing local or systemic spread of infection
- Pain control

Non-pharmacological Treatment

- Socket debridement
- Irrigation of the socket
- Patient is instructed to rinse with warm saline (5ml spoonful salt in 200mls cup of warm water) or 3% hydrogen peroxide.

Pharmacological Treatment

- Antibiotics
    - **Amoxicillin 500mg** (PO) 8 hourly for 5–7 days PLUS Metronidazole 500mg (PO) 8 hourly for 5-7 days.
- Pain management: **Paracetamol or NSAID**s can be used

REFERRAL

- If symptoms persist for more than a week with the above management, the patient needs to be referred to a hospital with maxillofacial surgical service.

Further reading

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21.4.3 DRY SOCKET (ALVEOLAR OSTEITIS) (AO)

BRIEF DESCRIPTION

- In some patients after extraction the clot formed get lost early impairing subsequent granulation and healing.
- Dry socket or alveolitis ostetis is a disturbance in healing that occurs after the formation clot but before the blood clot is replaced with granulation tissue.
- Excess fibrinolysis appears to be the main pathophysiologic mechanism.
- It is very painful condition.

CLINICAL FEATURES

Symptoms

- Severe pain in the vicinity of the extraction site, onset 2- 5 post-extraction
- The pain is usually difficult to control with commonly use analgesics
- Unpleasant taste or mouth odor

Signs

- Tenderness of alveolar socket wall
- No clot or necrotic tissue in the socket

INVESTIGATION AND DIAGNOSIS

- The diagnosis of dry socket is based on the presence of typical clinical manifestations (severe pain and bad odor)

TREATMENT

Objectives of treatment

- Pain management
- Enhancing clot formation

Non-pharmacologic treatment

- Socket debridement and irrigation with saline or 3% hydrogen peroxide, to be repeated for subsequent 2-4 days in an attempt to initiate clot formation.

PHARMACOLOGIC TREATMENT

- Local anesthesia during debridement and irrigation, 2% Lidocaine.
- Pain management: Tramadol, NSAIDS or a combination can be used.
- Antibiotics are not indicated.

FURTHER READING

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2. S. Preetha. An Overview of Dry Socket and Its Management. IOSR Journal of Dental and Medical Sciences .Volume 13, Issue 5 Ver. II. (May. 2014), PP 32-35
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21.5 TOOTH ERUPTION, SHEDDING AND EDENTULOUSNESS

21.5.1 TEETH ERUPTION DISORDERS

- Eruption of deciduous /primary teeth usually starts at about five months of age.
- Symptoms associated with eruption like fever and diarrhea are common and self-limiting.
- Eruption cyst
- An eruption cyst (EC) is a benign, developmental cyst that accompanies an erupting primary or permanent tooth, forming shortly before the tooth's appearance
  - An eruption cyst appears as a soft, translucent, dome-shaped lesion filled with blood or a clear fluid overlying the crown of an erupting tooth.
  - In most cases, EC subsides spontaneously; therefore, close monitoring is the standard of care
  - If it does not subside surgical therapy (simple excision of the cyst and exposing the crown)

21.5.2 SHEDDING OF DECIDUOUS/ PRIMARY (MILK) TEETH

- Shedding is physiologic phenomenon of loosing of deciduous/primary teeth which occurs at about the age of 5-12 years.
- Deciduous/primary teeth should be left to fall out on themselves unless the teeth are carious or there is any other indication.
- Parents should be counseled accordingly and be instructed to assist their children to loosen the tooth that is already mobile
- When there is no success or the permanent teeth are erupting in wrong direction a dentist should be consulted.

21.5.3 EDENTULOUSNESS

- Edentulousness is a partial or full loss of natural teeth and subsequent resorption of the alveolar bone.
- Treatment: It is by designing and constructing dental prosthesis according to aesthetic and functional needs.
- Refer patients for proper prosthesis treatments

21.5.4 MALOCCLUSIONS

- Malocclusion is any variation in the arrangement of teeth leading to abnormal occlusion with functional impairment or aesthetically unacceptable.
- There are several forms of malocclusion
- Malocculsion is assessed using a check list: the malocclusion of check list
- Treatment aims at reducing the following
  - Temporomandibular joint pain dysfunction
  - Traumatic dental and gum injuries
  - Caries
  - Psychosocial impact (low self-esteem, decreased social acceptability)
  - Appliances are the main stay of treatment of malocclusion

21.6 ORAL MUCOSAL CONDITIONS

21.6.1 APHTHOUS ULCERS (RECURRENT APHTHOUS STOMATITIS, RAS)

BRIEF DESCRIPTION

- Aphthous ulcers (RAS) are painful mucous membrane ulcerations with a tendency to be recurrent.
- It can affect any part of the non-keratinized part of the oral mucosa.

- Classification of recurrent aphthous ulcers

Table 21.2 Classification of recurrent aphthous ulcers (RAS)

	Minor	**Major**	**Herpetiform**
Size	<10mm (3-10mm)	>10cm	2-3mm
Number	1-5	1-10	10-100
Morphology	– Round or oval – Pseudomembrane – Erythematous halo	– Round or oval – Pseudomembrane – Erythematous halo	– Small – Deep ulcers that converge – Irregular contour
Localization	– Non-keratinized mucosa – Tounge, lips, cheeks, floor of the mouth	– Keratinized and non-keratinized mucosa – Soft palate and pharynx are commonly involved	– Nonkeratinized mucosa – Lips, cheeks, floor of the mouth, gums
Healing with scarring	No	Yes	No
Duration	1-2 weeks	2weeks to 3 months	1-2 weeks

CLINICAL FEATURES

Symptoms

- Pain around the lesions is the main symptom: causing difficulty in taking or eating
- Systemic symptoms like fever are not present.

- Recurrence is characteristically present

Signs

- Lesions are characteristic: single or multiple, different size, discrete, rounded, and white to yellow exudate in the middle with erythematous surrounding centrally.
- Location of lesion: any part of the oral mucosa can be involved
- Heal without scarring

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of RAS is made based on clinical grounds.
- All patients with major RAS need to be screened for HIV
- Bechet disease should be strongly considered in patients in patients with RAS with or without genital ulcers.
- Further investigation depends on the presence of other systemic features e.g. screening for Crhon's disease if there are GI symptoms

TREATMENT

Objectives of treatment

- Pain control
- Prevention of recurrence
- Prevention of secondary infection

Non-pharmacologic treatment

- Oral hygiene
- Avoidance trauma to mucosa: Braces, bitting, hard foods

Pharmacologic management

- **Minor RAS**
  - Triamcinolone acetonide paste 0.1%, apply 12 hourly for 5days

Alternative

- If topical steroid is not available and pain persists systemic steroid can be given. Prednisolone 20-40mg/day for 05 days

- **Major RAS**
  - Needs specialist evaluation
  - Start short course prednisolone 20-40mg/day and refer

REFERRAL

- **Patients** with major RAS, refractory lesions and those with systemic symptoms should be referred.

FURTHER READING

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2. Tarakji B, Gazal G, Al-Maweri SA, Azzeghaiby SN, AlAizari NA. Guideline for the diagnosis and treatment of recurrent aphthous stomatitis for dental practitioners. J Int Oral Health 2015;7(5):74-80.
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21.6.2 CANDIDIASIS, OROPHARYNGEAL (THRUSH)

BRIEF DESCRIPTION

- Oropharyngeal candidiasis, or thrush, is a common local infection.
- Common risk factors are extremes of age (infants or elderly), dentures, inhaled steroids, antibiotics, immunosuppressive therapy, HIV infection, diabetes, chemotherapy or radiation therapy
- The most common etiology is Candida albicans, but other nob-albian species might also cause thrush.

CLINICAL FEATURES

- The clinical features depend on the clinical type , shown in the table below

21.3 The clinical features and the clinical type of Candidiasis, oropharyngeal (Thrush)

Clinical types of acute oral candidiasis	Clinical types of chronic oral candidiasis	Additional candida associated oral lesions
Pseudomembranous	Pseudomembranous	Angular cheilitis
Erythematous (atrophic)	Erythematous (atrophic)	Denture stomatitis
	Hyperplastic	Median rhomboid glossitis

SYMPTOMS

- Oral candidiasis can be asymptomatic
- Some patients might have burning/tingling sensation
- Dysphagia might indicate esophageal involvement.

Signs

- **Pseudomembranous**
    - White creamy, curdled milk like patches on any part of the oral cavity(tongue, palate, buccal mucosa, oropharynx)
    - Easily scrapable to expose the underlying erythematous mucosa
- **Erythematous (atrophic)**
    - Erythematous and depapillated tongue, erythematous buccal mucosa
- **Hyperplastic**
    - It is either nodular or plaque like, usually located on the cheek mucosa and tongue

  - The lesions are not easily detached by scrapping making it difficult to differentiate from leukoplakia.
- **Angular cheilitis**
  - Erythema, thickening, and maceration on one or both corners of the mouth.
- **Denture stomatitis**
  - Chronic erythema and edema on the mucosa beneath the dentures
- **Median rhomboid glossitis**
  - A flat or raised well circumscribed, usually rhomboid shape, erythematous area on the dorsal surface of the tongue.

Investigations and diagnosis

- The diagnosis is made on clinical grounds based on risk factors and recognition of the lesions.
- KOH or gram stain on from scraping the lesions shows budding yeasts with or without hyphae.

TREATMENT

Objectives of treatment

- Achieve clearance of lesions
- Prevent spread
- Improve symptoms

Non-pharmacologic treatment

- The underlying risk factor should be addressed, if reversible e.g. ART for HIV patients

Pharmacologic management

- **Topical therapy:** For mild disease

- Miconazole oral gel 25mg/ml, 2.5 mL (1/2 tea spoon) of gel, applied four times a day after meals for 7-14 days. The gel should not be swallowed immediately, but kept in the mouth as long as possible, for at least one minute before swallowing.

  OR

- Clotrimazole troches, 10 mg, 5 times daily for 7-14 days

- **Systemic therapy:** For moderate to severe disease or for mild disease with failed topical therapy
  - Fluconazole, PO, 100–200 mg daily, for 7–14 days

REFERRAL

- Patients with disease refractory to fluconazole should be referred.

FURTHER READING

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21.6.3 HERPES SIMPLEX GINGIVOSTOMATITIS

BRIEF DESCRIPTIONS

- A common viral infection commonly affecting the lips and perioral soft tissue,
- It is caused by herpes simplex virus type 1 (HSV-1).

- Primary herpetic gingivostomatitis typically occurs in children.
- After the primary infection the virus stays in the trigeminal ganglia in a latent state.
- Reactivation occurs following exposure to sunlight, cold, trauma, stress, or immunosuppression
- HSV1 spreads by saliva
- Recurrence can occur in the buccal mucosa (recurrent stomatitis) or on the lips (herpes labials)
- It can rarely spread to other organs to result in life or organ threatening complications e.g. encephalitis, pneumonitis, keratitis

CLINICAL FEATURES

Symptoms

- Age range 6 month – 5 year
- Fever and constitutional symptoms
- Patients with recurrent lesions might feel a prodrome of tingling sensation, pain around the mouth before
- Poor appetite

Signs

- The lesions begin as vesicles and coalesce to form painful ulcers
- Lip adhesions
- Swollen and bleeding gingiva
- Regional lymphadenopathy

INVESTIGATIONS AND DIAGNOSIS

- The diagnosis of gingivostomatitis usually is made clinically based upon the typical appearance.

TREATMENT

Objectives of treatment

- Enhance early clearance of lesion
- Pain control
- Prevent complications

Non-pharmacologic management

- Hydration: encourage oral hydration

Pharmacologic management

- **Antiviral therapy**
  - Indications of antiviral for primary lesions
    - Presentation within four days of onset
    - Presentation after four days but still has significant symptoms or new lesions
  - **Systemic antiviral for primary HSV lesions**
    - **Acyclovir 400mg** PO every 8hours for 5-7 days (child: 20 mg/kg/dose 4 times daily for 5 -7 days. Maximum 400mg/dose)
  - **Topical antiviral for primary HSV lesions**
    - Topical antiviral have not been found to be consistently useful
    - **Topical Acyclovir** can be added in immunosuppressed individuals:Acyclovir cream or ointment 5%, applied 5 times/day
  - **Indications for antivirals in recurrent lesions**
    - Recurrent lesions are milder and do not require antiviral therapy.
    - In patients who have a clear prodrome systemic antiviral (Acyclovir tablet) is indicated: it should be started before appearance of the lesion
- **Pain and fever management**: Paracetamol or NSAIDS

FURTHER READING

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2. P. Chayavichitsilp, J. Buckwalter V, A. C. Krakowski, S. F. Friedlander. Herpes Simplex. Pediatrics in Review Vol.30 No.4 April 2009.
3. Ching-Chi Chi . Herpes labialis. Clinical Evidence 2015;10:1704.

21.7 TRAUMATIC DENTAL INJURIES

BRIEF DESCRIPTION

- Trauma to the teeth or the jaw may result in loosening, displacement and/or loss of teeth, fracture of teeth and or bone, lacerations and bleeding.
- The most common affected teeth are upper incisors.
- Dental injuries
    - **Tooth concussion**: injury to supporting tissues of tooth, without displacement.
    - **Subluxation**: partial displacement, loosening of a tooth without displacement
    - **Luxation**: displacement of tooth (laterally, labially, or palatally).
    - **Intrusion**: Displacement of tooth into its socket, often accompanied by fracture of alveolar bone
    - **Crown fracture**: fracture on visible part of the tooth portion
    - **Root fracture**: traumatized root of the tooth
    - **Avulsion**: complete fall of the tooth out of its socket by trauma.
- Lost (avulsed) tooth should be recovered for replantation

- If a permanent tooth is avulsed, it should be recovered and transported for replantation.
- Do or advise the following
    - Keep the patient calm.
    - Find the tooth and pick it up by the crown (the white part).
    - Avoid touching the root.
    - If the tooth is dirty, wash it very briefly (maximum 10 seconds) under cold running water and reposition it.
    - Encourage the patient to replant the tooth and bite on a cloth to hold it in position.
    - If the patients is not fully conscious or very young children. The following are possible ways of transportation of a tooth
        - A glass of milk
        - Inside the cheek or lip
        - Saliva (spit in to a container and keep it)
        - Normal saline

- Soft tissue injuries
    - Abrasion: superficial, denuded epithelium, and occasionally involves deeper layer.
    - Contusion: is more commonly called a bruise, tissue disruption with subcutaneous or submucosal hemorrhage without a break in the soft tissue surface.
    - Laceration: is a tear in the epithelial and sub epithelial tissues. It is commonly by a sharp object.

EVALUATION OF DENTAL TRAUMA

- Check for facial fractures and trauma to other sites, rule out evidence of head Injury (amnesia, loss of consciousness, neurological signs)
- Intra-oral examination: Look for soft-tissue lacerations, dental fractures, alveolar fractures and damage to teeth.
- Check for tooth fragments which may be displaced in soft tissues
- Examine traumatized teeth for mobility and check mobility
- X-rays: periapical x-ray for suspected root fracture, and OPG x-ray for suspected alveolar bone fracture and jaw fracture.

TREATMENT

- Tetanus anti-toxoid (TAT): see section on tetanus
- Suture : soft tissue wounds
- Wash mouth: warm saline solution or 3% hydrogen peroxide solution. Repeat mouth wash 3 times daily.
- Pain management: paracetamol or NSAIDS
- Give prophylactic antibiotics
- Prophylactic antibiotic: if there is extensive tissue damage with gross contamination
  - **Amoxicillin** 500 mg, PO, TID for 5 days
- Efforts should be made to save the permanent tooth unless there is root fracture.
- Restoration of aesthetics (composite filling, prosthesis).
- Extraction: it is treatment of choice for significantly traumatized primary/ deciduous teeth with mobility and or displacement.

REFERRAL

- Refer to a dentist, where available orthodontics or endodontic specialist
- Referral to oral and maxillofacial surgeon is needed when patients have maxillofacial injuries

FURTHER READING

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CHAPTER 22:

OBSTETRICS, GYNAECOLOGY AND FAMILY PLANNING

22.1 OBSTETRIC CARE AND OBSTETRIC DISORDERS

22.1.1 HYPERTENSIVE DISORDERS IN PREGNANCY

BRIEF DESCRIPTION

- Hypertension is a common medical problem that complicates pregnancy.
- It may be manifested as chronic hypertension, chronic hypertension with superimposed pre-eclampsia, pregnancy induced hypertension, pre-eclampsia or eclampsia.

CLINICAL FEATURES

- Increased BP≥ 140/90 mmHg during pregnancy. Measured 4 hours apart and after 20 weeks of gestational age.
- The presence of other clinical signs and symptoms of hypertension in pregnancy depends on the severity of the disease.

INVESTIGATIONS

- The presence of significant proteinuria greater than 300mg/24hour urine specimen or, less accurately, or more than 1+ protein (equivalent to approximately 100mg/dl) on dipstick sampling of random urine specimen.
- Proteinuria is usually late manifestation of pre-eclampsia that follows the hypertension and correlates with glomerular lesions in the kidneys.'
- Proteinuria is usually variable and should be carefully interpreted because it can be influenced by factors like contamination of the urine specimen with vaginal secretions, blood, or bacteria; urine specific gravity, pH,

exercise; and posture.

CLASSES

I. PREGNANCY INDUCED HYPERTENSION (PIH)

- Pregnancy induced hypertension is defined as a rise in BP> 140/90 mmHg after the 20th week of gestation measured twice at least four hours apart or a single measurement of diastolic BP>110mmHg, except in Gestational Trophoblastic Diseases (GTD) and multiple pregnancy when this can be diagnosed before the 20th week of pregnancy. There are different types of PIH.

A. GESTATIONAL HYPERTENSION

- This is diagnosed when the systolic BP is raised to 140 mmHg and the diastolic BP to 90 mmHg or more after the 20th week of gestational age without significant proteinuria. Mostly, this is used until a more specific diagnosis can be assigned. Gestational hypertension may represent pre-eclampsia prior to proteinuria or chronic hypertension previously unrecognized.

B. PRE-ECLAMPSIA

- Pre-eclampsia is part of PIH which is defined as a BP ≥ 140/90mmHg in the presence of significant proteinuria of ≥ 300 mg/24 hours urine specimen or, less accurately, more than 1+ protein (equivalent to approximately 100mg/dl) on dipstick in at least two randomly collected urine specimen at least 6 hours apart after the 20th week of gestation/ or up to 6 weeks postpartum.

C. SEVERE PRE-ECLAMPSIA/ WITH SEVERITY FEATURES

- In the presence of any one of the following clinical manifestations, severe pre-eclampsia can be diagnosed:
- Diastolic BP ≥ 110 mmHg and the systolic ≥160mmHg measured twice at least six hours apart or a single measurement of ≥120mmHg.
- Hyperbilirubinemia, Hemolytic anemia, Thrombocytopenia (<100,000/μl), Elevated Liver Enzymes (HELLP syndrome).

- Disseminated Intravascular Coagulation (DIC).
- Headache, visual disturbance and right upper abdominal pain.
- Oliguria (<400ml in 24hours or 30ml/hour).
- Cardiac decompensation, pulmonary edema, cyanosis.
- Exaggerated Deep Tendon Reflexes (DTR)

D. ECLAMPSIA

- Eclampsia is the occurrence of convulsions in woman who meets the diagnostic criteria for pre-eclampsia. There could also be atypical eclampsia. Any convulsion occurring during pregnancy is eclampsia unless proven otherwise.

II. CHRNIC HYPERTENSION

- This is a hypertension existing before pregnancy or diagnosed before the 20th week of gestation/ up to 6 weeks postpartum, or persists indefinitely after delivery. Women with mild hypertension may have normal BP during the mid-trimester and many of these women show greater decrease in their BP during pregnancy than normotensive women. However, in some pregnant women the BP may become severe and develop superimposed pre-eclampsia, which is defined as an exacerbation of the BP, i.e., an increment of the systolic BP by 30 mmHg and diastolic BP by 15mmHg over the baseline with development significant proteinuria.

PREVENTION:

- Women with the following risk factors for pre-eclampsia can benefit from taking low dose aspirin, 81mg, oral, daily starting from 12 weeks of gestation onwards:
    - Pre-eclampsia in the previous pregnancy
    - Family history of pre-eclampsia (in mother or sister)
    - Multiple pregnancy
    - Chronic hypertension
    - Renal disease

- Diabetes mellitus
- Anti-phospholipids syndromes or Systemic lupus erythematosis (SLE)
- Raised BMI

TREATMENT

Objectives

- Control BP by administering potent anti-hypertensive medicines, to keep the diastolic BP below 100 mmHg.
- Prolong pregnancy as much as possible
- Prevent convulsion
- Monitor maternal and foetal condition frequently for worsening of disease condition and plan treatment accordingly.
- Assure delivery of the fetus and placenta at the appropriate time, which is the definitive treatment for PIH.

Non pharmacologic

- Bed rest at home in the lateral decubitus position. Individuals rarely require admission unless they develop any sign and symptom of severe pre-eclampsia.
- Frequent evaluation of foetal wellbeing by foetal movement recording, biophysical profile
- Maternal wellbeing (BP measurement four times per day, assessment LFT, RFT, Hematocrit, proteinuria, visual disturbances, epigastric pain etc.)
- Advise patient to immediately report whenever they develop symptoms of severity such as headache, epigastric pain, blurring of vision etc.
- Plan termination of pregnancy at term. Most authorities recommend pregnancy to be terminated between 37-38 weeks of gestation.
- If the disease progresses to severe range, manage as severe case.

PHARMACOLOGIC

- Anti-convulsant such as Magnesium Sulphate, as well as anti-hypertensive medications, are rarely required for patients on conservative management. However, if the Systolic BP is >150mmHg or the diastolic BP is above 100mmHg, give:
- **Methyldopa**, 250-500mg P.O., 8 to 12 hourly

Alternative

- **Nifedipine**, 10-40mg P.O., 12hourly

OR

- **Nifedipine,** slow release 30-60mg P.O., daily

Note: Advise patient to immediately report whenever they develop severe symptoms such as headache, epigastric pain, blurring of vision etc.

SEVERE PRE-ECLAMPSIA

- **Delivery** is the appropriate/definitive treatment for mothers with severe pre-eclampsia; other-wise it may pose significant risks to the mother and fetus.

OBJECTIVES

- The primary objective is**,** to forestall convulsions, prevent intracranial bleeding and other vital organ damage and deliver a healthy fetus.
- Lower the BP but should not be under 140/90mmHg.
- Stabilize the mother and plan delivery.
- Lower the BP to a mildly hypertensive level (diastolic BP between 90-100mmHg)

Non pharmacologic

- Meticulous measurement of input and output is important part of the management.

- All non-pharmacologic measures for mild pre-eclampsia mentioned above should be applied here.
- Delivery: The vaginal route of delivery is preferable as long as there are no contraindications.

Pharmacologic

- **Control of hypertension**: The ideal medicine for this clinical scenario is the one that reduces the BP in a controlled manner, avoiding precipitous reduction in BP that may compromise placental perfusion.

First line

- **Labetalol,** 20-50mg intravenously is a useful second line medicine for women whose hypertension is refractory to hydralazine.

Alternative

- **Hydralazine,** 5-10mg intravenous every 20 minutes whenever the diastolic BP≥ 110mmHg. As hydralazine has duration of action of several hours, adequate control of severe hypertension is often achieved after one or two intravenous treatments.

OR

- **Nifedipine**, 10 mg sublingual whenever the diastolic BP ≥ 110mmHg.

PREVENTION OF CONVULSION

First line

- **Magnesium sulphate,** A loading dose of 4gm as 20% solution IV over 10-15 minutes followed by 10gm as 50% IM injection divided on two sides of the buttock, followed by maintenance dose of 5gm every 4 hours as 50% concentration over 2minutes, 2gm IV as 50% solution over 2minutes if convulsion recurs. Reduce the maintenance dose by half if there are signs of renal derangement during labour and for the first 24 hours postpartum.
- **Management of Magnesium toxicity:** If DTRs are depressed, discontinue MgS04 and monitor the patient closely.

- **Treatment: Calcium gluconate** (if respiratory rate below 12/min), 1 gm. as 10% in 10 ml ampoule IV over 2 minutes.
- **Caution**: administration of MgSo4 should be with caution in the face of renal failure, decrease the maintenance dose by half or use alternative medication.

Alternative

- **Diazepam,** 30 IU/1000ml of D/W or D/S 20 drops /minutes and increase the drops as needed depending on the patient's sedation status.

Note: Continuous infusion is unnecessary because the half-life of the medicine is 18 hours. When the maternal dose exceeds 30mg neonatal side-effects become prominent. These include low Apgar score, respiratory depression, poor feeding and hypothermia.

TREATMENT OF ECLAMPSIA

Objectives

- Prevent maternal injury
- Control convulsion: Control the acute fit and prevent further recurrence
- Control extreme hypertension
- Expedite delivery
- Prevent patient from falling

Non pharmacologic

- Turn patient on her side to minimize aspiration
- Apply mouth gag to prevent tongue injury
- Establish airway and administer adequate oxygen
- Catheterization

PHARMACOLOGIC

- The same as for severe pre-eclampsia (see above). In addition broad spectrum antibiotics should be given to prevent aspiration pneumonitis./ as prophylaxis for aspiration pneumonia.

Note:

- Do not give Furosemide as part of the treatment for hypertension unless there is pulmonary edema.
- Do not give ACE-inhibitors anti-hypertensives, such as captopril, as they may damage the developing fetus.

POST-PARTUM MANAGEMENT

- The first 48-hour postpartum period is critical as one in three fits can occur during this period. No management should be altered during this period.
    - Check BP and urine protein frequently
    - Discontinue anti-convulsants within 48 hours
    - Follow the mother for 6 weeks

22.1.2 HYPEREMESIS GRAVIDARUM

BRIEF DESCRIPTION

- Nausea and vomiting are common complaints in the first trimester of pregnancy and is considered by many as diagnosis of pregnancy. The symptoms are severe in multiple gestations and gestational trophoblastic neoplasm. Protracted vomiting associated with dehydration, starvation, weight loss, electrolyte disturbances, acidosis and ketonuria is known as hyperemesis gravidarum.

CLINICAL FEATURES

- Excessive vomiting, loss of appetite, sign of dehydration, low BP, increase pulse rate, weight loss
- In severe cases acidotic pattern of breathing (deep and shallow) may ensue.
- In addition the clinician should look for other medical and surgical causes like hyperthyroidism, food poisoning, diabetes, appendicitis, etc.

INVESTIGATIONS

- Ketonuria, Elevated AST and ALT
- Screen the patient for UTI and other medical causes
- Ultrasound examination to look for GTD, Multiple gestation

TREATMENT

Objectives

- Adequate fluid, electrolyte and calorie replacement
- Arrest the vomiting with potent anti-emetics
- Manage hypovolemic shock if present
- Identify obstetric conditions that are associated with hyperemesis garvidarum
- Out other medical or surgical causes, e.g., UTI, malaria, appendicitis etc.

Non pharmacologic

- For uncomplicated nausea and vomiting of pregnancy, give reassurance.
- Advice on small, dry, high calorie frequent feeding
- Avoid fatty and spicy foods
- Emotional support
- Remove stressful home environments
- Withdraw oral nutrition and fluid for 24-48 hours
  - Women with nausea should eat before, or as soon as, they feel hungry to avoid an empty stomach, which can aggravate nausea.

PHARMACOLOGIC

Majority of Hyperemesis gravidarum cases requires admission for inpatient care. Few mild cases can be treated as outpatient.

- Correct dehydration with up to 2 L intravenous Ringer's lactate infused over three to five hours, supplemented with appropriate electrolytes and vitamins.
- Subsequently, the infusion rate is adjusted to maintain a urine output of at least 100 mL/hour and the solution is changed to dextrose 5% in 0.45% saline.
- Avoid use of dextrose in the initial rehydration fluid because of the theoretical concern of Wernicke's encephalopathy with dextrose infusion in a thiamine-deficient state.
- Calorie replacement: Add 40% Glucose 2 vials (40 ml) in each bag.
  - 12 vials of 40% dextrose/400calories/24hrs
- Add Vitamin B complex 3 ampoules in each bag

CONTROL OF VOMITING:

First line

- **Chlorpromazine**, 12.5-25 mg I.M. BID until vomiting is controlled and then P.O.

Alternatives

- **Promethazine,** 25-50 mg IM/IV BID, followed by 25 mg P.O., BID. Maximum daily dose,100mg

OR

- **Metoclopramide,** 5-10 mg IV/IM BID or TID.

OR

- **Pyridoxine hydrochloride**, oral, 25mg/day, every 8 hour.

In severe and refractory cases:

- **Dexamethasone**, IM/IV, 4-8mg daily

PLUS

- **Ondansetron**, IV 4-8mg over 5minutes daily

Note: If these fail to control the vomiting, pregnancy may be terminated.

22.1.3 PAIN DURING LABOUR AND DELIVERY

BRIEF DESCRIPTION

- When giving analgesics and anesthetics to pregnant mothers, the safety of the mother and fetus should be of constant concern to the health care provider. Virtually all analgesics and anesthetics administered during pregnancy cross the placental barrier, though to different extent; thus, a balance must be sought between pain relief for the mother and safety of the fetus.

TREATMENT

Objectives

- Alleviate pain without affecting maternal and foetal condition

Non pharmacologic

- Hypnosis, attention focusing and distraction
- Maternal movement and change of position: when the mother moves she alters the relationships between gravity, uterine contractions, the fetus and her pelvis.
- Counter pressure: Steady and strong force applied to a spot on the lower back during contraction or pressure on the side of each hip.
- Hot compresses applied to the lower abdomen.
- Immersion in warm water during labour but not birth

PHARMACOLOGIC

Analgesics

- Opioids

First line

- **Pethidine, 50**-100mg IV or IM QID to TID.

Alternatives

- **Morphine**, 10-15mg IM, TID

  OR

- **Pentazocine**, 30mg IM/IV
- **Local Anesthetics**
- The **complete relief of pain** in obstetrics can be accomplished by **blocking the sympathetic pathways of eleventh and twelfth thoracic nerve**s and the parasympathetic and sensory fibers of the sacral nerves.
  - Epidural **block:** is a more effective form of pain relief than alternative forms of analgesia.

First line

- **Bupivacaine**, 3-5mg of 0.75% in 8.25% dextrose.

Alternative

- **Lidocaine (Xylocaine)**, 1-2% concentration IM, 5-10ml

22.1.4 POST-PARTUM HEMORRHAGE (PPH): PREVENTION AND MANAGEMENT

BRIEF DESCRIPTION

- **Post**-partum hemorrhage refers to bleeding of more than 500ml from the genital tract within the first 24 hours of normal delivery or any amount of blood loss that compromises the hemodynamic of the patient which is referred as primary.
- It usually occurs during or immediately after the third stage of labour.
- Secondary post-partum hemorrhage is defined as excessive vaginal

bleeding occurring from twenty-four hours to six weeks after delivery.

- Postpartum hemorrhage becomes life threatening if the mother is already anemic.

CAUSES

- Uterine atony
- Retained product of conceptus in the uterine cavity
- Infection within the uterine cavity (endo-myometritis)
- Birth canal injury
- Clotting disorders

RISK FACTORS FOR PPH

- Suspected or proven abruptio placentae
- Known placenta previa
- Multiple pregnancy
- Pre-eclampsia/Gestational hypertension
- Previous history of PPH
- Anemia
- Big baby

CLINICAL FEATURES

- Excessive or prolonged vaginal bleeding
- Lower abdominal pain, supra-pubic tenderness
- Bleeding from the genital tract
- Conjunctival pallor
- Rapid pulse rate
- BP may be low or normal

INVESTIGATIONS

- CBC
- Coagulation profile (PT, PTT, INR)
- Liver function test
- Renal function test
- Blood grouping and cross-matching
- Ultrasound scan

Prevention:

- Every woman is considered a potential risk for PPH, hence active management of the third stage of labour must be applied, i.e., from the time of delivery of the fetus until the delivery of the placenta. Active management of third stage of labour, is a series of procedures applied during the third stage to speed up the delivery of the placenta, increase uterine contractions to prevent PPH by averting uterine atony. It has the following components:
  - To give oxytocin within one minute after the birth of the baby without waiting for sign of placental separation. OR Ergometrine, IM, 0.2mg, provided the woman is not hypertensive.
  - Clamping and cutting the cord as soon as the baby is delivered.
  - Apply Controlled Cord Traction (CCT) when the uterus becomes globular and firm and the cord lengthens.
  - Continuous uterine massage, repeated every 15 minutes for 2 hours
- *Note:* Despite these measures, if bleeding continues, management of PPH should be started immediately.

TREATMENT

Primary PPH

- **Objectives**
  - Identify the causes

  - Arrest bleeding as quickly as possible
  - Resuscitate patient

Non-pharmacologic

- The following management options should be applied step by step:
  - Continuous rubbing of the uterus
  - Ensure the urinary bladder is empty
  - Call for help
  - If the placenta cannot be expelled in this fashion within 30 minutes, do manual removal, preferably under anesthesia.
  - If bleeding continues or is heavy which lead to derangement of the vital sign; start blood transfusion, a minimum of 2 units.
  - If the placenta has been delivered and is incomplete, explore the uterus under general anesthesia.
  - If the placenta is complete and the uterus is well contracted: examine the patient with adequate analgesia and/or anesthesia, any lacerations in the cervix or vagina, must be sutured using through-and-through sutures. If the tear extends into the uterine body, it would be difficult to suture it from below and laparotomy may be required for effective suturing.
  - For ruptured uterus, repair or hysterectomy should be done.
  - Avoid dextrans; they interfere with blood grouping and cross matching as well as with coagulation of blood.
  - If bleeding continues despite uterine rubbing, employ interventions such as manual compression of the uterus and compression of the abdominal aorta, use condom tamponade or uterine packing.
  - If bleeding continues despite the above mentioned measures: Bilateral internal artery ligation or B-Lnych procedures can be applied.
- *Note:* If all the above measures fail, resort to hysterectomy SOONER rather than LATER, especially in cases of placenta accreta or uterine rupture.

Pharmacologic

First line

- **Oxytocin,** IM, 10 units stat.

Alternative

- **Misoprostol**, oral/sublingual, or rectal 600-800micrograms. Subsequently, maintain uterine contractions by massaging the fundus and infusing **Oxytocin**, IV, 10 units in 500 ml 5% Glucose in sodium chloride 0.9%. Anesthesia for manual removal of placenta **Pethidine** IV, 100mg and **Diazepam** IV, 10 mg

OR

- **Ketamine**, IM/IV bolus or infusion, 6-10 mg/kg
    - Set up IV infusion of Sodium Chloride 0.9% to run in fast: First 1000 ml rapidly in 15-20 minutes. Give at least 2000 ml in first hour. Aim to replace 2-3x the volume of estimated blood loss. If condition stabilizes then adjust rate to 1000 ml /6 hourly

OR

- **Oxytocin**, infusion, 20 IU in 1L of Normal saline

OR

- **Ergometrine**, 0.25mg P.O., 8hourly for 3 days

SECONDARY PPH

Objectives

- Identify the cause and treat appropriately
- Prevent overwhelming infection

Non pharmacologic

- Resuscitate the patient
- Explore the uterus for retained product of conceptus

Pharmacologic

- Use of the uterotonic agents is similar as to primary PPH

Antibiotics

- Amoxicillin-**Clavulanic acid**, IV, 1.2 gm, 12hourly ***OR*** Ampicillin 2 gm IV QID

  PLUS

- Gentamicin, IV/IM, 80mg, 8hourly

  PLUS

- Metronidazole, IV, 500mg, 8hourly

  OR

- Clindamycin, IV, 450mg, 8-12hourly
  - When the clinical condition of the patient improves the IV antibiotics changed to PO.

22.1.5 PREMATURE RUPTURE OF MEMBRANES (PROM)

BRIEF DESCRIPTION

- Premature rupture of membranes is rupture of the foetal membranes after the 28th week of gestation and before onset of labor.
- The amniotic fluid surrounding the fetus is important for the development of foetal lung and limb, heat exchange, and protection of the umbilical cord and infant from compression.
- In addition, the amniotic fluid has bacteriostatic chemicals.
- Whenever the membranes rupture, there will be leakage of fluid; hence these protective mechanisms may be compromised.
- In addition, if a dent is created a portal of entry will be established for bacteria to access the amniotic fluid from the vagina.

- Rupture of membranes often leads to onset of labor.
- Thirty- five percent of preterm neonates result from preterm PROM.

CAUSES

- Preterm labour, trauma, infection

CLINICAL FEATURES

- Gush of fluid per vaginum.
- Sterile speculum examination reveals leakage of clear or greenish fluid through the cervical opening.
- If immediate delivery is not planned, vaginal digital examination is not advisable.

INVESTIGATIONS

- Microscopic examination of the fluid reveals; Foetal products (squamous cells), fat, lanugo hair, fibronectin, AFP, prolactin) Ferning test (arborization).
- Nitrazine paper test which changes from yellow to dark blue. But care should be taken as blood, semen, alkaline urine and vaginal infections can give false positive results.
- Ultrasound examination: for assessing amniotic fluid, GA, foetal weight
- Vaginal swab culture and sensitivity for group B streptococcus

CLASSES

- **Pre-term PROM:** Rupture of membrane before 37th week of gestation
- **Term PROM:** Rupture of membrane after 37th week of gestation
- **Prolonged PROM:** Rupture of membranes for more than 8 hours

TREATMENT

- Treatment depends on the gestational age, presence of infection, condition of the fetus and spontaneous healing of the membrane.

Objectives

- Prevent or early detect for sign of chorioamnionitis by clinical means (uterine tenderness, malodorous amniotic fluid, fever, maternal and foetal tachycardia) and laboratory (increase WBC, C - reactive protein).
- Prolong pregnancy until foetal maturity is assured, i.e., until 34 weeks and above.

TYPES OF PRE-TERM PROM AND THEIR MANAGEMENT

1. Preterm PROM without chorioamnionitis

Non pharmacologic

- Admit
- Bed rest and IV hydration
- Avoid vaginal examination,
- Avoid coitus
- Closely follow indications of intra-amniotic infection.

Pharmacologic

First line

- **Ampicillin**, 2gm IV QID for 48 hours followed by 500mg P.O., QID or 7-10 days.

PLUS

- **Erythromycin**, 500mg IV QID for 48 hours followed by Erythromycin 500mg P.O., QID for 7-10 days. ***OR*** Azithromycin 1gm PO stat at admission.

2. Pre-term/Term PROM with chorioamnionitis

- Admit to the labor ward and facilitate delivery as feasible.
- Use ampicillin, chloramphenicol or gentamicin and terminate pregnancy.

First line

- **Ampicillin,** 2gm IV QID for 48 hours followed by 500mg P.O., QID or 7-10 days.

PLUS

- **Gentamicin**, 80mg intravenously TID

OR

- **Chloramphenicol**, 500-1000mg intravenously QID

3. **Term PROM with no evidence of chorioamnionitis**

- Admit to the labor ward and follow for evidence of infection
- If labour does not start spontaneously after the latency period, induce labour with oxytocin.

4. **Prolonged PROM:**

- **Ampicillin,** 2gm I.V. QID during labor until she delivers, then 500 mg QID for 7 days.

22.1.6 PRETERM LABOUR

GENERAL DESCRIPTION

- Preterm labor can be defined as regular uterine contractions that cause progressive dilatation of the cervix after 28th weeks of gestation and before 37 completed weeks.
- Approximately 8-10% of all pre-pregnancies end in preterm labour.
- Prematurity is one of the major causes of perinatal mortality and morbidity.

CAUSES

- The etiology of preterm labor is multi-factorial, including;
  - Multiple gestation
  - Infection like UTI, febrile illness, abdominal surgery

- Uterine anomalies, APH (placenta previa and abruptio placentae)
- PROM
- Low socioeconomic status

CLINICAL FEATURES

- Pushing down sensation in the mother and if the clinician detects regular rhythmic uterine contraction of four in 20 minutes or eight in 60 minutes that leads to progressive cervical dilatation and effacement.
- Cervical dilatation greater than 2 cm
- Cervical effacement of 80 percent or greater

Investigation

- CBC
- FBS
- Transvaginal ultrasound can show cervical dilatation and effacement
- Fibronectin in vaginal secretion

TREATMENT

- When the diagnosis of preterm labour is made, the medical team should attempt to determine the cause and whether further continuation of the pregnancy will be beneficial or harmful to the mother and fetus.
- The choice of treatment depends on the answer to these questions and maturity of the fetus.
- Once foetal maturity is assured there is no benefit to conservative management and pregnancy should be terminated through the safest route.
- But if the fetus is premature, conservative management should be attempted.

Objectives

- Prevent or detect early intrauterine infection

- Prolonged pregnancy until foetal maturity is achieved
- Promote foetal lung maturity by administering corticosteroids
- Treat any underlying causes e.g., UTI, malaria, pyelonephritis etc.

Non pharmacologic

- Bed rest
- Oral hydration, especially with nutritive calories, such as fruits juices, milk etc.
- Circlage

Pharmacologic

- Use of a **tocolytic medicine** is not associated with a clear reduction in perinatal or neonatal mortality or neonatal morbidity.
- The main effect of tocolytic medicines when used for women in preterm labour is to reduce the numbers who deliver within 48 hours or within 7 days after the medicine administration.
- Data on long-term outcome are sparse.
- It remains plausible that, for selected women, such as those who require transfer for neonatal care or time to complete a course of corticosteroids, there may be benefits associated with tocolysis.
- However, the benefits have not been formally evaluated in randomized trials.
    - **N.B.** There is no benefit from maintenance tocolytic therapy.
- **Nifedipine**, initial 20mg orally, followed by 10-20mg three to four times daily, adjusted according to uterine activity for up to 48 hours; a total dose of 60mg appears to associated with 3-4-fold in adverse events such as headache and hypotension.

PLUS

- **Steroid therapy** for stimulation of surfactant production to be given 28-34weeks of gestation

First line

- **Betamethasone**, two doses of 12mg IM 24 hours apart. After 48 hours from the first dose, the full effect on maturing the surfactant has been obtained.
    - If patient does not deliver within one week, the treatment should be repeated if the fetus is less than 34 weeks of gestation.

Alternative

- **Dexamethasone,** 6mg P.O./IM for two doses six hours apart for two doses.
    - *Note:* Use of corticosteroids in the presence of infection is contraindicated
- **Sympathomimetics:** Ritodrine and salbutamol are associated with significant; potentially life-threatening maternal side effects (particularly if given in combination with corticosteroids) which include fluid overload, pulmonary edema, myocardial ischemia, hyper or hypoglycemia, hence, these combinations should be abandoned totally in the management of preterm labour.

22.1.7 PROLONGED PREGNANCY

BRIEF DESCRIPTION

- The terms "Prolonged, post-date and Post-term pregnancy" which are synonymously used, to define pregnancy that exceeds 42 weeks (294 days), from the day since the last menstrual period.
- The incidence of post-term pregnancy averages 4-5%.
- Post-term pregnancy may be complicated by foetal post maturity, macrosomia, oligohydramnios, meconium aspiration syndrome and placental insufficiency due to placenta ageing.
- Management of post pregnancy can take two forms; either expectant management with foetal surveillance, or elective induction of labour.
- **Induction of labour** is any attempt to initiate uterine contractions

before the spontaneous onset of labour to facilitate the expulsion of conceptus product.

CLINICAL FEATURES

- Prolonged pregnancy is diagnosed from the last menstrual period or ultrasonography done in early pregnancy.
- Prolonged pregnancy may manifest with foetal macrosomia or IUGR, decrease foetal movement, decrease amniotic fluid.

INVESTIGATIONS

- Ultrasonography
- Cardiotography
- Biophysical profile
- Foetal movement
- Non-stress test (NST) and Stress Test

Treatment

Objectives

- Prevent maternal birth trauma and operative deliveries
- Prevent perinatal morbidity and mortality
- Assess risk factors before any intervention
- Asses the inducibility of the cervix

INDUCTION OF LABOUR

- This is one option of treatment of prolonged pregnancy, but before induction is attempted the cervix must be favourable, the bladder must be empty and the following risk factors should not be present in the pregnant woman:
  - Previous scar on the uterus (C/S, myomectomy etc.)
  - Cephalopelvic disproportion (CPD)

  - Malpresentation or malposition
  - Non re-assuring FHB pattern
  - Placenta previa

Non pharmacologic induction of labour

- Breast stimulation:
- Amniotomy (artificial rupture of membrane)
- Stripping of membrane (digital separation of the membranes from the lower uterine segment)
- Mechanical methods: iinsertion of Laminaria or Foley catheter into the cervical canal.

PHARMACOLOGIC INDUCTION OF LABOUR

- **Oxytocin**
  - It is administered intravenously in different ways ranging from simple manually adjusted, gravity-fed systems, through mechanically or electronically controlled infusion pump, to fully automated closed-loop feedback systems.

DOSAGE SCHEDULE

- **Low dose regimen**

- For **primigravida**, 5 units in 1000ml N/S to run at 20drops/min (2mU/min), double the drop every 20 minutes until adequate contraction is achieved to maximum of 80 drops/minute, if adequate contraction could not be achieved with the maximum dose add 5 units to the same bag and start the drop from 40/minute, if there is no adequate contraction with this dose add 5 units more to the same bag to a maximum dosage of 64mU/min.

- **For Multigravida:** Use half of the dose for primigravida women.
- **High dose regimen**

  - Start with 6mU/min and increase the dosage by 6mU/min every 15 minutes until adequate contraction is achieved to maximum of 64mU/min for primigravida and 32mU/min for multigravida.

- **Prostaglandins**
  - Vaginal or cervical applications of PGs (E2, F2α and E1) are widely used for cervical ripening. They are administered intra-vaginally and intra-cervically.
  - **Dosage:** PGE2 3mg into the posterior fornix six hours apart for 2 doses followed by administration of oxytocin 12 hours later

ADVANTAGES OF ADMINISTRATION OF PGE2 FOR CERVICAL RIPENING

- Enhances cervical inducibility
- Decreased need for oxytocin for induction
- Decrease oxytocin induction time and dosage
- Decreased C/S rate related to failed induction

22.1.8 PROLONGED LABOUR

BRIEF DESCRIPTION

- The labor is said to be prolonged when the combined duration of the first and second stage is more than the arbitrary time limit of 18 hours.
- The causes of prolonged labour could be cephalopelvic disproportion (CPD) or insufficient uterine contraction in terms of frequency, duration and strength.
- The treatment of prolonged labour depends on the cause.
- If prolonged labour is due to inefficient uterine action the treatment is augmentation of labour using oxytocics.

PHARMACOLOGIC AUGMENTATION

- Is any attempt to stimulate uterine contractions during the course of labour to facilitate the expulsion of the fetus. But cephalopelvic disproportion should be excluded before augmentation. Dose half of that of Induction.

CLINICAL FEATURES

- The frequency of uterine contraction is less than three in 10 minutes, duration is less than 30 seconds and weak contractions.
- This can be assessed clinically by palpating the uterus or using an intrauterine that measures the intrauterine pressure.

INVESTIGATIONS

- Ultrasound
- CTG
- Doppler

TREATMENT

Objectives

- Prevent uterine rupture
- Prevent foetal distress and IUFD
- Carefully assess for side effects of oxytocin

Pharmacologic

- The only pharmacologic agent available thus far is oxytocin

22.2 COMMON MEDICAL DISORDERS IN PREGNANCY

22.2.1 ANEMIA IN PREGNANCY

BRIEF DESCRIPTION

- Anemia secondary to iron deficiency is the commonest medical disorder in pregnant women, particularly in the developing countries.

- Anemia is one of the major indirect causes of maternal death.
- Anemia in pregnancy is defined as when the Hemoglobin (Hgb) level is below 11gm/dl in the first and third trimesters and below 10.5gm/dl in the second trimester of gestation. The causes of anemia are the same as in non-pregnant period. Iron demand is increased by a factor of 4-5times during pregnancy.

CLASSES

- **Mild anemia**: when the hemoglobin level is 8-11gm/dl
- **Severe anemia**: when the hemoglobin level is < 7gm/dl

CLINICAL FEATURES

- Nonspecific symptoms like weakness, dizziness, palpitation, shortness of breath.
- Physical examination may reveal significant pallor of the conjunctiva and other parts of the body.

INVESTIGATIONS

- CBC, Hgb/Hematocrit
- Peripheral RBC morphology
- Bone marrow aspiration
- Stool examination for hookworm infestation
- Blood film for malaria
- RFT, LFT

TREATMENT

- Treatment depends on the severity of anemia and the underlying medical and obstetric condition of the mother.

Objectives

- Correct the anemia as urgently as possible before the patient goes to labour.

- Identify the cause of anemia like hookworm infestation, malaria etc.

A. Mild to moderate anemia

Non pharmacologic

- Iron-rich diet
- Minimize hemorrhage during pregnancy and childbirth

Pharmacologic

First line

- Ferrous **sulphate**, 325 mg PO TID with food.

PLUS

Folic acid, 5 mg Po daily

B. Severe anemia: Requires admission and blood transfusion in the presence of complications.

Refer: if the anemia is severe (Hgb <7gm/dl) refer patient for further investigation and fast correction of the anemia.

22.2.2 JAUNDICE IN PREGNANCY

BRIEF DESCRIPTION

- Jaundice occurring in pregnancy may be a sign or symptom of a severe disease and should be considered seriously.

CAUSES

Obstetric

- Severe pre-eclampsia/eclampsia/HELLP Syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets syndrome)
- Severe hyperemesis gravidarum
- Intrahepatic cholestatic of pregnancy
- Acute fatty liver of pregnancy

Non-obstetric

- Viral hepatitis (E, B and C)
- Hemolytic jaundice due to malaria, septicemia, medicines and herbal medications
- Surgical causes of jaundice; acute cholecystitis, cholelithiasis, obstructive jaundice

CLINICAL FEATURES

- Severe pruritis, malaise, anorexia, vomiting, jaundice, RUQ abdominal pain, fever, headache

Investigations

- CBC, Blood film for malaria parasites and peripheral morphology
- Group and cross matching
- Renal function test, liver function tests, serum electrolytes
- Bile acid level, lipid profile, Hepatitis B surface antigen
- Abdominal ultrasound
- Abdominal CT scan

TREATMENT

- Treatment essentially depends on the underlying cause of jaundice.
    1. ***Severe pre-eclampsia (HELLP) syndrome****…….refer specific topic above*
    2. ***Hyperemesis gravidarum****……………..refer specific topic above*
    3. ***Acute fatty liver of pregnancy* (AFLP):**
- It is common in obese multiparous women to experience multiple gestation in their third trimester of pregnancy.
- This is due to defect in the mitochondrial fatty acid beta oxidation; fatty acids and later triglycerides accumulate in the liver and impair its function.

CLINICAL FEATURES

- AFLP should be considered in any pregnant woman presenting with one or more of the following:
    - Epigastric pain, symptoms suggestive of reflux esophagitis, nausea, vomiting, jaundice
    - Bleeding diathesis even in the absence of hepatic encephalopathy.
    - 50% patients will show signs of pre-eclampsia.

INVESTIGATIONS

- CBC, uric acid, bilirubin, liver function test, bile acid
- Hepatitis B and C test

TREATMENT

Objective

- Prevent grave complications
- Terminate pregnancy at the appropriate time

Non pharmacologic

- Bed rest
- Strict measurement of BP, blood sugar level and coagulation status and electrolyte
- If there is DIC: Transfuse fresh frozen plasma, fresh blood, platelet
- Termination of pregnancy

22.2.3 INTRA-HEPATIC CHOLESTASIS PREGNANCY (IHCP)

BRIEF DESCRIPTION

- IHCP occurs from late second trimester to third trimester of pregnancy.

- Common in women of advanced age, multiparous, previous personal or family history of IHCP.
- It is diagnosed when otherwise unexplained pruritus occurs in pregnancy and abnormal liver function tests (LFTs) and/or raised bile acids occur in the pregnancy.
- Pruritus that involves the palms and soles of the feet is particularly suggestive.
- Other causes of itching and liver dysfunction should be excluded before labeling the woman as suffering from IHCP.
- Women with persistent pruritus and normal biochemistry should have LFTs repeated every 1–2 weeks.
- Typically, jaundice develops 2-4 weeks after the debut of pruritus. Postnatal resolution of the pruritus and the abnormal LFTs should be confirmed.
- It is associated with preterm labour, foetal distress and meconium staining liquor, and still birth.

CLINICAL FEATURES

- Generalized pruritus which mainly affects the palm and sole and severe at night, jaundice, pale stool and dark urine.

INVESTIGATIONS

- Same as AFLP

TREATMENT

Objectives

- Alleviate symptoms
- Differentiate the disease from other cholestasis causes: intra-hepatic (viral infections) and extra-hepatic (e.g., cholelithiasis)

Non pharmacologic

- Termination of pregnancy alleviates the symptoms

Pharmacologic

- There is no evidence that any specific medicine treatment improves foetal or neonatal outcome. However, the following medicines can be tried to alleviate the pruritus;
    - Topical emollients: Calamine lotion
    - Systemic medicines
    - Chlestyramine, P.O., 20mg/day
    - Anti-histamines, e.g, chlorpheniramine
    - Vit. K

22.2.4 CARDIAC DISEASES IN PREGNANCY

BRIEF DESCRIPTION

- The commonest causes of cardiac disease in pregnancy are secondary to rheumatic heart disease followed by the congenital ones, in the ratio of 10:1 respectively.
- Due to the increase in cardiac output during pregnancy, patients with underlying cardiac disease can be decompensated easily, particularly near 28 weeks of gestation, during labour and immediate postpartum period, hence women with severe heart disease will benefit immensely from preconception counseling.
- On the other hand, due to these hemodynamic changes, normal pregnant patients may report signs and symptoms that may mimic cardiac disease; hence, differentiation of normal from abnormal is difficult.
- The severity of heart disease is assessed according to the classification of the New York Heart Association (NYHA), which by and large depends on the response of the heart to physical activities, not the extent of cardiac lesion.
    - Class I: Asymptomatic at all degrees of activity: uncompromised

  - Class II: Symptomatic with ordinary activities: slightly compromised
  - Class III: Symptomatic minimal exertion: markedly compromised
  - Class IV: Symptomatic at rest; incapacitated.

CAUSES

- Rheumatic heart disease
- Hypertension
- Cardiomyopathy
- Anemia
- Congenital heart diseases
- Hyperthyroidism

CLINICAL FEATURES

- Progressive dyspnea or orthopnea, nocturnal cough, hemoptysis, syncope, chest pain, cyanosis, clubbing of fingers, persistent neck distension, systolic murmur grade 3/6 or greater, diastolic murmur, cardiomegaly, persistent arrhythmia etc.

INVESTIGATIONS

- ECG, Echocardiography, CXR, CBC, Blood urea and electrolytes
- Thyroid function test, when indicated
- Other ante-natal investigations

TREATMENT

- A cardiologist, obstetrician and pediatrician should work as a team in the treatment of these patients.

Objectives

- Avoid aggravating factors
- Treat exacerbating factors: thyrotoxicosis, anaemia, infection etc

- Prevent or detect cardiac decompensation early

Non pharmacologic

- Early diagnosis and arrange evaluation by a specialist
- Early booking and assessment for severity of the disease
- Bed rest and limitation of activities
- Reduce cardiac work load: restrict fluid intake, reduce tachycardia, correct anaemia
- Avoid supine position in late pregnancy
- Apply elastic stocking to the lower leg to prevent pooling of blood
- Assist vaginal delivery by instruments to shorten the second stage of labour
- Put patient in propped up (semi-fowler's) position.

PHARMACOLOGIC

Antepartum

- Treatment **of congestion:** diuresis
    - ○ **Frusemide**: start with low dose and increase dose as per response; **Frusemide** 20 mg Po daily and dose adjustment following response.
- Heart **rate control:** beta blockers
    - ○ **Metoprolol** 12.5 mg daily and escalate dose as per the response

Alternative

- **Propranolol**, 40mg P.O., TID
- **Digoxin**: indicated with reservation (same dose as that of non-pregnant women)
    - ○ To control the heart rate in atrial fibrillation
    - ○ To suppress some other supra-ventricular tachcardias

  - To increase the force of contraction

ANTI-COAGULANTS FOR

- Valvular heart disease with fibrillation
- Prosthetic heart valves

First trimester

- **Unfractionated heparin**, IV, 5000 units as bolus, followed by 17,500 IU SC BID (If perfussor is available: run 1000 IU per hour)
- **Unfractionated heparin**, SC, 10,000-15000 units 12hourly. The dose must be adjusted to achieve mid-target a PTT at 2-3x of the control

Second trimester

- **Warfarin**, 5mg daily. Control with INR to keep within the therapeutic range of 2.5–3.5.

After 36 weeks until delivery

- **Unfractionated heparin**, IV, 5000 units as bolus, followed by 17,500 IU SC BID (If perfussor is available: run 1000 IU per hour)

OR

- **Unfractionated heparin**, SC, 10-15,000 units 12hourly. Adjust dosage to keep the aPTT 2-3 times of the control.
- **During labour**
  - Check BP, PR and RR half-hourly.
  - Keep the woman in a sitting or lateral position.
  - Do relevant cardiac examination at least 4 hourly.
  - Strict fluid balance chart should be used.
  - Continuous electronic FHB monitoring is recommended.
  - Advice mother not to push and allow descent only by contractions
  - Vaginal delivery should be in propped up position

- Oxygen (5-6L/min) with face mask should be provided if needed (e.g. Cyanosis, PAH, MI).
- Invasive hemodynamic monitoring and pulse oximetry - if indicated
- Vaginal delivery is the preferred route.
- Reduce labour pain by giving epidural anesthesia or pethidine 50-100mg, IM/IV with promethazine 25-50mg, IM
- Oxygen, 5-6L/min, through nasal catheter
- Broad spectrum antibiotics to prevent SBE: Gentamicin, 80mg IM/IV TID and Ampicillin 1g, IV/IM TID at the onset or induction labour.
- Stop heparin on the morning of elective caesarean section or when there is an established labour, restart heparin 6hours after vaginal delivery or 12 hours after caesarean section

- **Post-partum**
    - The first one hour is critical because of the remobilization of the fluid into the vascular bed.
    - Ergometrine should be avoided especially if the lesion is tight mitral stenosis or an Atrio- Ventricular (AV) shunt, because it may precipitate pulmonary edema.
    - Post-partum hemorrhage, anemia, infection and thromboembolism can precipitate Heart Failure and should be managed accordingly.
    - Hospital stay at least 48 hrs. after delivery.

22.2.5 DEEP VEIN THROMBOSIS/ THROMBOEMBOLISM (DVT/PTE) IN PREGNANCY

BRIEF DESCRIPTION

- The adaptation of the maternal hemostatic system to pregnancy predisposes women to an increased risk of venous thromboembolism.

- Pregnancy produces the components of Virchow's triad, including an increase in vascular stasis, changes in the coagulation system, and vascular injury.
- That is why pregnancy is said to be thrombogenic.
- It is not surprising that venous TE is a potential risk of complication of pregnancy and puerperium, because the incidence of TE is five times higher than non-pregnant patients.
- Venous thrombo-embolism (VTE) can manifest in three forms: Superficial thrombophlebitis which can be treated with analgesics, elastic support and rest, deep vein thrombosis (DVT) and pulmonary thrombo- embolism (PTE).
- These forms represent spectrum of diseases, as one form may progress to the next.

CLINICAL FEATURES

- **Superficial thrombophlebitis:** hot, red and tender area in relation to a superficial vein.
- **DVT**: Clinical presentation vary, from severe pain and edematous white leg (phlegmasia alba dolens) to being asymptomatic, manifesting with pulmonary thrombo-embolism only.
- **Pulmonary thrombo-embolism (PTE):** Acute chest pain, breathlessness, cyanosis, and hemoptysis may be accompanied by hypotension and collapse.

INVESTIGATIONS

- Compressional ultrasound of peripheral veins
- Doppler ultrasound

TREATMENT

Objectives

- Liquefaction of the already formed thrombus
- Prevent further propagation of thrombus

- Prevent PTE
- Prevent recurrence of thrombosis
- Prevent long term complications, including venous insufficiency, pulmonary hypertension, right sided Heart Failure, post-thrombotic syndrome

Non pharmacologic

- Elevation of legs
- Apply a graduated elastic compression stocking to reduce leg edema
- Encourage ambulation while graduated compression stocking applied

Pharmacologic

- **Heparin,** IV, in the order of 5,000-10,000IU, followed by17,500 IU SC BID (if available:1000-1200IU/hour, and should be administered in saline through an infusion pump.

Followed by

- **Warfarin,** 2.5-5mg/day, excluding the first trimester up to the 36weeks of pregnancy.

POSTPARTUM:

- Therapeutic anticoagulants should continue for at least 6 weeks.
- Warfarin should be avoided until the third day or longer in women at increased risk of PPH.

22.2.6 DIABETES MELLITUS COMPLICATING PREGNANCY

BRIEF DESCRIPTION

- Diabetes is one of the most common medical problems that complicate pregnancy.
- Diabetes in pregnancy can be gestational or pre-gestational.
- Women with pre-gestational diabetes need to have preconception

counseling to achieve good glycemic control at the time of conception and organogenesis to avoid congenital abnormality.

- Women with gestational diabetes mellitus become normoglycemic immediately, but a significant number of them can become diabetic if followed for long period of time.
- Diabetes in pregnancy, if not well controlled, may cause many obstetric and non-obstetric complications that include;macrosomia,polyhydramnios, congenital anomalies, maternal hyper or hypoglacemia depending on the gestational age, UTI, hypertension, exacerbation of retinopathy etc.
- **Types of diabetes in pregnancy**:
    - Gestational Diabetes Mellitus
    - Pre-existing type I and II Diabetes mellitus
- **Gestational Diabetes Mellitus (GDM)** is a carbohydrate intolerance of variable severity with onset or first recognized during pregnancy.

CLINICAL FEATURES

- Usually it is asymptomatic and identifications of the risk factors is important.

INVESTIGATIONS

- **Screening;** by administering 50gm glucose load and determine the blood glucose level one hour later.
- If the value is more than 140mg/dl, the woman needs Oral Glucose Tolerance Test (OGTT) using 100gm anhydrous glucose which is a confirmatory test.
- According to the American Association of Diabetes women with the following risk factors should be screened for GDM between the gestational age of 24-28 weeks.
- Family history of DM in the first sibling (mother, father, sister or brother)
- Obese (BMI >27)
- Mothers above the age of 35 years

- Race (being black)
- Previously, in addition to the above-mentioned risk factors, the following were included as a screening criterion; previous delivery of macrosomic fetus (>4kg), previous pregnancy complicated by GDM, unexplained foetal losses, persistent glucosuria, but if the screening is based on these criteria, 50% of pregnant women prone to being diabetic can be missed.

Table: 22.1. Upper limit for normal glucose level (mg/dl) in OGTT

Sample	Fasting	1st hour	2nd hour	3rd hour
Whole blood	90	165	145	125
Plasma	105	190	165	145

ADDITIONAL INVESTIGATIONS

- Ultrasound: between 16-22 weeks for congenital anomalies, at 32 weeks for foetal size
- CBC
- Urinalysis, urine culture and sensitivity
- Vaginal swab for candidiasis
- Renal function tests and electrolytes
- Liver function tests
- FBS and 2 hours post-prandial every 2-4 weeks
- HgbA1c every 2-3months

TREATMENT

Objectives

- Maintain good glycemic control, i.e, the fasting plasma glucose level to be < 105mg/dl and the two hours post-prandial <120mg/dl.
- Prevent maternal and foetal complications.
- Prevent neonatal morbidity

- Minimize long term complication of diabetes

Non pharmacologic

- **Diet:** most women with GDM can be managed with diet alone.
    - Three meals and 3-4 snacks/day
    - Diet with 40-50% carbohydrate, 20% protein and 30-40% fat content.
    - 10% of calorie at breakfast, 30% at lunch and dinner and 30% with snack.
    - Heavy meals must be avoided
- **Exercise**
    - Walking or exercise using the upper part of the body is recommended.
    - Mild to moderate exercise, preferably non-weight bearing, at least 3 times/week is recommended.
    - Avoid exercise in the supine position after the first trimester
    - Exercise is contraindicated in the presence of the following conditions:
        - Pregnancy induced hypertension
        - Rupture of membrane
        - Preterm labour
        - Cervical incompetence
        - Vaginal bleeding
        - Intrauterine growth restriction (IUGR)

Pharmacologic

- **Insulin**, 0.5 units/kg in the first half of pregnancy and increase the dosage to 0.7units/kg in the second half. This is the average dosage otherwise the dose requirement may vary from individual to individual.
- By splitting injection to 2/3 in the morning (as 2/3 long-acting and 1/3 short-acting) and 1/3 in the evening (as 1/2 long-acting and 1/2 short-

acting) good blood glucose control should be achieved.

- Combination of 1/3 short and 2/3 intermediate acting insulin is used to maintain the FBS to 60-90mg/dl 1-hour post-prandial values at<120mg/dl.

FOLLOW UP

- Fasting blood glucose and 1 hour postprandial every 2-3 weeks
- HgbA1c every 2-3months
- There is no place for urine glucose determination in the management of diabetes in pregnancy except for screening.

DELIVERY

- Unless there are other obstetric contraindications, induction of labour and vaginal delivery is the preferred route of delivery.
- If the blood glucose control is satisfactory with diet and exercise, follow the pregnancy until term with close foetal surveillance until spontaneous onset of labor. But if the blood glucose control is unsatisfactory, plan delivery after ascertaining the lung maturity using shake test, laminar bodies count etc.

INTRA-PARTUM/INTRA-OPERATIVE GLYCEMIC MANAGEMENT:

- Withhold the AM insulin injection for planned delivery
- Start IV infusion with 5% D/W at 100ml/hour
- Start Insulin infusion with regular insulin at 0.5units/hour
- Monitor maternal glucose levels hourly and adjust insulin infusion accordingly
- Closely follow the foetal heartbeat

POST-PARTUM MANAGEMENT:

- The need for insulin declines in post-partum period, therefore adjust the dose based on sliding scale. Insulin may not be required the first 24-48 hours for gestational and type II diabetes patients. For type I diabetes check the blood glucose every 2 hours and follow the scalding scale.

- If the blood glucose level becomes normal, OGTT should be done at the 6th post- partum week.
- Newborn should be assessed for the following risks:
    - **Hypoglycaemia:** This can be prevented by initiating immediate breast feeding, or, by giving **Dextrose** 10%, IV, 4ml/kg body weight as bolus, followed by maintenance of 60ml/kg body weight in 24 hours.
    - Respiratory distress syndrome
    - Hyperbilirubinemia
    - Congenital abnormalities.
- Breast feeding should be encouraged.
- Encourage contraception with progestins or surgical sterilization.

22.2.7 TYPE I AND II DIABETES MELLITUS

BRIEF DESCRIPTION

- Many serious problems can ensue in women with type I and II diabetes during pregnancy.
- These complications are dependent on the presence of vascular problems which in turn are dependent on the duration of the diabetes.
- Based on this concept the White's classification (classes A-F) is used to predict outcome, though, the predictive value of this classification is less precise in modern management.
- All women with type II on oral hypoglycemic agents in the pre-pregnancy period must be shifted to insulin.

- If hypertension combines with diabetes, it is an ominous sign.
- Therefore, the BP should be closely monitored.

CLINICAL FEATURES

- The same as those for GDM

TREATMENT

Objectives

- Same as those of GDM

Non pharmacologic

- Same as that of GDM

Pharmacologic

- The pharmacologic treatment is the same as that of gestational diabetes mellitus.
- However, insulin requirement should be adjusted according to gestational age.
- Maternal hypoglycemia may occur in the first half of the pregnancy.
- Hence, the insulin should be slightly decreased from the pre-pregnancy dosage.
- Whereas on the second half of pregnancy the insulin resistance increases, typically between the gestational age of 20-30weeks, hence, the dosage of insulin should be adjusted accordingly.
- Sometimes, a decrease need to insulin may arise towards late pregnancy which implies that the placenta is failing to function which implies the insulin resistance is disappearing.
- This is an ominous sign for the fetus.

22.2.8 THYROID DISEASES IN PREGNANCY

BRIEF DESCRIPTION

- The thyroid gland produces T4 and T3 hormones in the ratio of 5:1. T3 is produced by peripheral conversion of T4 in a larger proportion.
- To produce this hormone the thyroid gland requires enough iodine.
- More than 95% of these hormones are found attached to thyroid binding globulin (TBG) in the circulation.
- The production of these hormones is controlled by TSH which is secreted by the anterior pituitary and this in turn is controlled by the negative feedback and TRH from the hypothalamus.
- The main function of the thyroid hormones (T3 and T4) are: energy production, stimulation of protein synthesis and facilitate growth in children.
- During pregnancy there is moderate enlargement of the thyroid gland due to its hyper- function.
- The TBG is markedly increases, almost doubles by the 12th week, proportionally, the T4 and T3 level also increases and the concentration of free hormone in the circulation is changed.
- There are different types of thyroid disorders in pregnancy:

HYPOTHYROIDISM

Clinical features

- Fatigue, hair loss, dry skin, excessive weight gain despite poor appetite, cold intolerance, muscle ache, stiffness, pain or tingling in the median nerve distribution due to carpal tunnel syndromes, low pulse rate, etc.

Investigations

- T4, T3 and TSH determination, ultrasound

TREATMENT

Pharmacologic

- **Thyroxin (T4)** 0.1mg every morning for one week and adjust the replacement dose to 2μg/Kg. Breast feeding is not contraindicated. Dosage should be reduced in the postpartum period.

22.2.8.1 HYPERTHYROIDISM

BRIEF DESCRIPTION

- Hyperthyroidism also causes anovulation and amenorrhea.
- In 95% of the cases thyrotoxicosis is due to Grave's disease but few could be due to solitary toxic adenoma or multinodular goiter or associated with obstetric conditions such gestational trophoblastic neoplasia.
- Foetal hyperthyroidism is one of the complications which may lead to neonatal hyperthyroidism, IUGR, intrauterine death etc.

CLINICAL FEATURES

- Family history of autoimmune thyroid disease, failure to gain weight despite good appetite, presence of exophthalmos or lid lag, persistent tachycardia, heat intolerance etc.

INVESTIGATIONS

- T4, T3, TSH and FTI. It is preferable to determine free T4 and T3,
- Fine needle aspiration

- Ultrasound
- Doppler ultrasound

TREATMENT

Objectives

- Identify the cause of hyperthyroidism
- Assess the severity of hyperthyroidism
- Prevent complications
- Manage appropriately to bring down to euthyroid level

Pharmacologic

First line

- Propylthiouracil, 150mg PO TID for 4-5 weeks. The dose is then progressively lowered to maintenance dose of 150 mg per day.

Alternative

- Carbimazole, 15mg TID for 4-5 weeks. The dose is then progressively lowered to maintenance dose of 15mg per day.

Thyroid crisis (storm)

- Thyroid crisis is a rapid worsening of thyrotoxicosis brought about by stress such as infection, labour and surgery. This scenario is common in women whose thyrotoxicosis is not well controlled, but it can occur also in well treated women.

CLINICAL FEATURES

- Fever, tachycardia, extreme nervousness, restlessness and psychosis, eventually may lapse into coma.

Investigations

- Free T3, T4,
- Ultrasound

TREATMENT

Non pharmacologic

- Reduce fever by tepid sponging or covering in wet sheet or turning on electric fan.
- Prevent aspiration

Pharmacologic

First line

- **Propylthiouracil,** 1000 mg orally initially, followed by 200mg QID.
    - ***Note:*** Administration of either of the antityroid medicines is followed by administration of sodium or potassium iodide, 500mg TID by infusion or orally QID to inhibit the release of thyroid hormone and Dexamethasone 2mg every QID for the first day to decrease the peripheral conversion of T4 to T3.
- **If the patient develops Heart Failure**; **Metoprolol** 0.5mg IV initial dose followed as orally in a dose of 25mg three times per day. The alternative is Propranolol 80 mg PO TID.
    - Follow heart rate and symptom control.
- **Chlorpromazine**, 25-50mg orally or intravenously 6-8hourly is administered to reduce fever.

***Note:* Aspirin** should not be used to reduce fever as it displaces thyroid hormones from TBG and thus increases the free hormones in the circulation, hence the condition could be worsened.

22.2.8.2 POSTPARTUM THYROIDITIS

BRIEF DESCRIPTION

- It is a well-recognized that 10-20 % of women develop some form of thyroid dysfunction in the postpartum period due to autoimmune diseases.

- Three quarters develop hyperthyroidism and the rest hypothyroidism in the 1–3-month postpartum period.
- Most of those who develop hyperthyroidism go into remission within 2-3 months but 30% will enter hypothyroid phase.

CLINICAL FEATURES

- Fatigue and palpitation, 50% will have goiter.

INVESTIGATIONS

- Fine needle aspiration-lymphocytic thyroiditis is the common finding.

TREATMENT

- **Hyperthyroid phase:** Anti-thyroid medicines are not indicated.
- **Hypothyroid phase:** Most of the time, it is self- limiting, but if symptoms are severe and prolonged, treatment with T4 is warranted.

22.2.9 HIV/AIDS IN PREGNANCY

BRIEF DESCRIPTION

- In the last 20-25 years HIV/AIDS has become a major indirect cause of maternal mortality.
- The majority of HIV positive women (77%) lives in Sub-Saharan Africa, and constitutes 57% of the global adult HIV positive population.
- Pregnancy by itself does not affect the course of the disease, but HIV may increase the risk of premature deliveries, small for date uterus and the rate of still birth.
- **Factors that influence MTCT include**: maternal viral load, nutritional status of the mother, presence of concomitant parasitic infection like malaria, severe immunodeficiency, advanced HIV/AIDS stage, presence of PROM and injury to the fetus and birth canal during labour and delivery.
- To reduce the rate of MTCT of HIV/AIDS, the Ethiopian government has adopted the four-pronged approaches in its PMTCT strategies, namely:

primary prevention, prevention of unintended pregnancy, prevention of HIV transmission from infected women to their infants, and treatment, care & support of HIV infected women, their infants and their families.

CLINICAL FEATURES

- Symptoms suggestive of opportunistic infections/malignancies or direct effects of HIV. History of seropositivity, history of HAART and other HIV/AIDS related illnesses, duration of illness, status of partner, WHO staging, any medication given for HIV-related illnesses since the beginning of pregnancy.

INVESTIGATIONS

- Serologic test for HIV after counseling. If she is HIV positive, carry out CD4 count, viral load, baseline tests such as CBC, RFT, LFT.
- Test for syphilis (VDRL), Hgb
- Test for opportunistic infections like TB

PREVENTION

- **HIV positive women who intend to get pregnant:** The following general health measures should be taken:
    - Adequate nutrition that includes: high calorie and food staff rich in iron, micronutrient supplementation such as iron, zinc and folic acid at least for three months prior to getting pregnant.
    - Prevention of malaria infection.
    - Prevention and treatment of STIs.
    - Prophylaxis and treatment of opportunistic infections.
    - Avoid pregnancy for at least six months following recovery from TB and other opportunistic infections.
    - Administer ART, if not already on treatment
- **During antenatal care (ANC)**
    - Advocate the benefits of VCT and persuade every pregnant woman to be tested.

  - If the pregnant woman turns out to be positive apply the primary preventive measures that include; early and appropriate treatment of STI, education about safer sex practice during pregnancy and lactation.

- **Intrapartum care: Labour and delivery:** These include avoiding invasive procedures, application of infection prevention and performing elective C/S on selected patients.

- **Post-partum care:** Avoiding breast feeding or exclusive breast feeding.

PMTCT clinical scenarios and ARV regimens: Refer the national guideline

> Note: Link the patient to PMTCT program and follow the updated national guideline.

22.2.10 URINARY TRACT INFECTION IN PREGNANCY

BRIEF DESCRIPTION

- **Urinary** tract infections (UTIs) are one of the most common medical complications of pregnancy. It is estimated that one in three women of childbearing age will have a UTI.

- Because of the normal physiologic changes induced by pregnancy, pregnant women are especially susceptible to UTIs, including asymptomatic bacteriuria, (no it is one risk factor not a clinical condition) we aim to treat asymptomatic bacteriuria for this particular reason cystitis and pyelonephritis. Urinary tract infection is common in women with diabetes.

CAUSATIVE ORGANISMS

- *E.coli* (most common, 75-90%), klebsiella, proteus, coagulase negative staphylococci, and pseudomonas

CLASSES

- Asymptomatic bacteruria

- Symptomatic UTI:

  - Lower UTI: Cystitis, urethritis
  - Upper UTI: Pyelonephritis

CLINICAL FEATURES

- Lower **UTI** (cystitis and uretheritis) will have supra-pubic tenderness, abdominal discomfort, hematuria, urgency, frequency, dysuria.
- Upper **UTI:** Flank pain (unilateral or bilateral) and abdominal pain, anorexia, nausea, vomiting, fever, chillness headache, dehydration, tachypnea

Investigations

- Urine analysis
- Urine culture: Growth of bacteria 105 organisms/ml of urine
- Blood culture when needed
- CBC
- BUN, creatinine
- Ultrasound

TREATMENT FOR ASYMPTOMATIC BACTERIURIA

Objectives

- Prevent pyelonephritis
- Identify the predisposing factors, if there is any, usually there is.
- Eradicate the infection and prevent recurrence

Non pharmacologic

- Take a lot of fluid and encourage frequent voiding.

Pharmacologic

- The treatment would be more rational if the choice of antibiotics is based on culture and sensitivity results.

First line

- Amoxicillin 500mg PO TID for one 7 days

Alternatives

- Cephalexin PO 500mg BID for 7days

Symptomatic lower urinary tract infections

- **Lower UTI (cystitis and urethritis)**
    - The symptoms are often difficult to distinguish from those due to the pregnancy itself.
    - Features that may indicate true infection include hematuria, dysuria, urethral discharge and supra-pubic discomfort.

Treatment

- **Treatment** is the same as asymptomatic bacteriuria.
- **Upper UTI (pyelonephritis)**
    - Acute pyelonephritis is a serious medical problem in pregnancy which requires admission and aggressive management.
    - Acute pyelonephritis could lead to complications like miscarriage, preterm rupture of the membranes, IUGR, preterm labour, intrauterine foetal death and sepsis.
    - The incidence increases with gestational age; 90% of the cases occur in the second and third trimesters of pregnancy and 20-40% follows asymptomatic bacteriuria.

TREATMENT

- Women with pyelonephritis require admission for parenteral medication.

Objectives

- Prevent foetal complications which include preterm labour, low birth weight, IUGR, PROM.
- Prevent maternal complication from, overwhelming urogenic sepsis, perinephric abscess, pre-eclampsia, acute renal failure.

- Identify the predisposing factors, including renal stone, congenital anomalies, diabetes mellitus.
- Prevent recurrence of UTI

Non pharmacologic

- Adequate nutrition and hydration
- Tepid sponging to lower fever

Pharmacologic

- The choice of antibiotics would be more rational, if it is based on culture and sensitivity.
- Antipyretics and analgesics, if tepid sponge is not effective in reducing fever.

First line

- **Ampicillin,** 2gm IV QID until 48 hours after the fever subsided and then 500mg P.O., for 10-14 days.

PLUS

- **Gentamicin,** 80mg IV TID until 48 hours after the fever subsided and then IM for 10-14 days.

Alternatives

- **Cephotaxime**, 500mg-1gm IV BID until 48 hours after the fever subsided and then continue IM BID for 7days

OR

- **Ceftriaxone,** IV, 1gm, BID, until 48hours after the fever subsided and then continue IM for 7 days.

OR

- **Cefuroxime**, IV, 750-1500mg, TID, until 48hours after the fever subsided and then continue P.O., BID for 7days.

22.2.11 SYPHILIS IN PREGNANCY

BRIEF DESCRIPTION

- **Syphilis** is a common sexually transmitted disease, which can cause significant intrauterine infection leading to abortion, pre-term birth, perinatal death and congenital anomalies.
- It is caused by a spirochete bacterium called *Treponema pallidum.*
- Routine screening is done at booking and at the third trimester of pregnancy, because it can infect the fetus at any point during gestation.

CLINICAL FEATURES

- Most mothers are asymptomatic.

INVESTIGATIONS

- Microscopy**:** by dark field examination or direct immuno-fluorescent Microscopy.

SEROLOGY

- Specific treponemal tests such as TPHA or FTA-Ab
- Nonspecific treponemal tests
  - o Venereal Disease Research Laboratory (VRDL) test
  - o The Rapid Plasma Reagent (RPR) test

TREATMENT

Objective

- Prevent long term and short term complications
- Prevent mother to child transmission

Pharmacologic:

First line

- Pregnant women with syphilis must be treated with **penicillin**, since no other medication effectively crosses the placenta to treat the fetus, even if allergic to penicillin must be desensitized and treated.

- **Benzathine penicillin** 2.4 Mil IU IM (1.2 Mil in each buttock) weekly for three consecutive weeks. Treat the partner similarly

Alternatives

- **Ceftriaxone** 1gm IM daily for 10 to 14 days
  - ***Note:*** Patients treated for syphilis in the second half of pregnancy can develop Jarisch- Herxheimer reaction, which can precipitate premature labor and foetal distress.

22.2.12 PELVIC INFLAMMATORY DISEASES (PID)

BRIEF DESCRIPTION

- Pelvic inflammatory disease (PID) is usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abscess and/or pelvic peritonitis.
- Sexually transmitted infections (STIs) are the main causative agents but anaerobes and other organisms from the lower genital and gastrointestinal tracts may also be implicated.
- PID could be post-sexually transmitted infection, post-partal and post-operative.
- It is caused by polymicrobial organisms such as *gonoccocus, chlamydia trachomatis, mycoplasma hominis and genitalium,* other intestinal and vaginal normal flora.

CLINICAL FEATURES

- The following clinical features are suggestive of a diagnosis of PID:

Major criteria

- Bilateral lower abdominal pain (sometimes radiating to the legs)
- Cervical motion/ excitation tenderness on bimanual vaginal examination

- Bilateral Adnexal tenderness on bimanual vaginal examination (with or without a palpable mass)

Minor criteria

- Fever (greater than 38°C)
- Abnormal vaginal bleeding (intermenstrual, post-coital or 'breakthrough')
- Deep dyspareunia
- Abnormal cervical or vaginal mucopurulent discharge
- Presence of abundant numbers of white blood cells (WBCs) on saline microscopy of vaginal secretions
- Elevated erythrocyte sedimentation rate
- Elevated C-reactive protein

INVESTIGATIONS

- WBC with differential count, ESR
- Culture and sensitivity of blood, pus, or vaginal discharge
- Vaginal Swab: excess WBC in wet mount smear may indicate PID
- RFT, LFT, electrolytes
- Ultrasonography
- Laparascopy for visualization of hyperemic tubes, purulent discharge (Gold standard): if feasible arrange referral or consult specialist

TREATMENT

Objectives

- Determine whether the patient can be treated as outpatient or requires hospitalization.
- Treat the acute infection: to eradicate the offending organism and prevent further dissemination of the infection.
- Prevent the damage of the fallopian tube which may lead to recurrent

infection, infertility, chance of ectopic pregnancy, chronic pelvic pain

Non pharmacologic

- Patient should refrain from sexual activities or douching.
- Consider removal of IUD if the woman is not improving with medication.
- Surgical management indicated if there is tuboovarian abscess(TOA) includes, laparatomy and drainage of abscess, salpingo- oopherectomy, colpotomy, hysterectomy with or without salpingo-oopherectomy

Pharmacologic

- **Outpatient treatment**

First line

- **Ceftriaxone,** 250mg IM single dose

  PLUS

- **Doxycycline**, 100mg P.O., BID.

  PLUS

- **Metronidazole,** 500mg P.O., BID for two weeks.

- **Inpatient treatment**

- **Inpatient** antibiotic treatment should be based on intravenous therapy which should be continued until 48 hours after clinical improvement and followed by oral therapy. Admission to hospital would be appropriate in the following circumstances:
  - If the diagnosis is uncertain
  - Clinically severe disease
  - Tubo-ovarian abscess
  - PID with pregnancy
  - PID in HIV positive women

- Lack of response to oral therapy
- Intolerance to oral therapy
- Poor compliance

First line

- **Ampicillin**, 500 – 1000mg IV, QID**,** followed by 500mg P.O., QID

  PLUS

- **Gentamicin**, 80mg, IV, TID followed by IM injection of similar dose

  PLUS

- **Clindamycin**, IV, 900mg, TID

  OR

- **Metronidazole**, 500mg IV TID followed by 500mg P.O., TID

Alternative

- **Ceftriaxone**, IV, 2gm/day, BID

  PLUS

- **Gentamicin**, IV, 80mg, TID

  PLUS

- **Metronidazole**, IV, 500mg TID Followed by either **Clindamycin** 300mg P.O., QID *OR*

- **Doxycycline**, 100mg P.O., BID

  PLUS

- **Metronidazole**, 500mg P.O., TID for 14 days
  - *Note:* In the outpatient setting, review of patient condition at 72 hours after initiation of medication is recommended, particularly for those with a moderate or severe clinical presentation

- In patients who have been on IV medication should continue oral treatment for 14 days after clinically being improved.
- In pregnancy, the physician should refrain from using Doxycline.
- Patients with PID wearing IUD: Consideration should be given to removing the IUD, especially if symptoms have not resolved within 72 hours.
- Women on hormonal contraception presenting with breakthrough bleeding should be screened for genital tract infection, especially for C. trachomatis.
- When a sexually transmitted infection is either proven or likely to be the cause of PID, the current sexual partner(s) should be traced and offered health advice and screening for gonorrhoea and chlamydia.

22.2.13 PUERPERAL MASTITIS

BRIEF DESCRIPTION

- Puerperal mastitis is breast inflammation that develops during the first month after delivery.
- Puerperal mastitis is a commonly encountered infection, hence early diagnosis and prompt management minimizes the impact on the mother and infant.
- Despite appropriate management, abscess formation occurs in 4-10% of cases. It is commonly caused by *Staph. aureus* and in some cases *Staph. epidemidis*.

CLINICAL FEATURES

- Fever, chills, flu like symptoms, breast pain with warm, erythromatous, indurated, engorged and tender breast (one or both breasts) and axillary lymphadenopathy. Fluctuating breast mass.

INVESTIGATIONS

- CBC
- Fine needle aspiration and Gram stain from the pus culture and medicine sensitivity from the breast abscess if any

TREATMENT

Non Pharmacologic

- Suctioning of the breast
- Breast-feeding with only the healthy breast
- Drainage of breast abscess
- Using supporting brassieres

PHARMACOLOGIC

- **Cloxacillin**, 500mg PO QID for 7-10 days. If there is evidence of sepsis, the patient requires hospitalization
- **Cloxacillin**, 500mg IV QID until the fever and clinical symptoms subside, and continue with oral Cloxacillin for 7-10 days.
    - ***Note:*** Do not wait until fluctuation; if there is induration, tap and confirm the diagnosis.

22.2.14 VAGINAL DISCHARGE SYNDROMES

22.2.14.1 BACTERIAL VAGINOSIS (BV)

BRIEF DESCRIPTION

- Bacterial vaginosis (BV) is a clinical syndrome characterised by the presence of malodorous vaginal discharge, with or without vaginal pruritus.
- Usually there is no external genital irritation or dysuria.

- The discharge is generally a homogeneous, non-viscous, milky white fluid which smoothly coats the vaginal mucosa and cervix.
- Imbalance of the normal vaginal flora is thought to play a role in the aetiology of BV, resulting in overgrowth of gardnerella, anaerobes, or genital Mycoplasmas.
- The absence of Hydrogen peroxide-producing Lactobacillus (maintain vaginal acidic PH) in the vagina appears to correlate with development of this disease.
- BV may cause adverse pregnancy outcomes like PROM, chorioamnionitis, preterm labour, premature birth, post-partum endometritis, and post-caesarean wound infection.

CLINICAL FEATURES

- Vaginal secretions characterized by at least three of the following: Amsel criteria for diagnosis of BV (at least three criteria must be present)
  - Amine ("fishy") odor before or after addition of 10% KOH solution.
  - PH ≥ 4.5 (unreliable if contaminated by menstrual bleeding or seminal secretions
  - Homogeneous, smooth, non-inflammatory discharge
  - Presence of clue cells (epithelial cells coated with bacteria) on microscopic examination.

Treatment

Objectives

- Alleviate symptoms
- Prevent adverse pregnancy outcomes following infection
- Avoid precipitating factors

Non pharmacologic:

- Avoid frequent douching

Pharmacologic

First line

- Metronidazole, 500mg P.O., BID for 7 days or 2g P.O., single dose

Alternative

- Metronidazole, 0.75% gel 5gm intra-vaginally QD for 5 days

OR

- Clindamycin 2% cream 5gm intra-vaginally, OR 300mg P.O., BID for 7 days OR 100mg intra-vaginally QHS for 3 days

In Pregnancy

- Metronidazole, 250mg P.O., TID for 7 days;

OR

- Clindamycin, 300mg P.O., BID for 7 days.
- **Sex Partners:** Routine treatment of male partners(s) with **metronidazole** does not prevent recurrence of Bacterial Vaginosis. For recurrent BV without evidence of other STD, use of condoms and avoiding douching is encouraged.

22.2.14.2 MUCOPURULENT CERVICITIS

BRIEF DESCRIPTION

- Mucopurulent cervicitis (MPC) has been called the female counter part of urethritis in males.
- It can be caused by sexually transmitted organisms namely *N. gonorrhoeae* or *C. trachomatis*, although in most cases tests are negative for both gonorrhea and chlamydia.
- The syndrome is characterized by muco- purulent cervical discharge and a cervical inflammatory response (friability, edema, ectopy, increased numbers of polymorphonuclear leukocytes (PMNs).
- However, presence of IUCD, Cervical ectropion (histologic diagnosis), oral contraceptives and menses may be associated with PMNs in endocervical

smears without MPC.

- Patients with MPC may note vaginal discharge, dyspareunia, post-coital or inter-menstrual bleeding, or other non-specific symptoms.

CAUSES

- Gonorrhea or Chlamydial infections
- Herpes cervicitis
- Trichomoniasis (ectocervicitis)

CLINICAL FEATURES

- MPC is diagnosed by the presence of criterion (a) below and at least one other criterion (b, c or d).
  a. Endocervical gram-stained smear with a monolayer of ≥ 15 PMNs/1000 X (oil immersion) field, (in a specimen obtained from the endocervix with a swab to wipe the cervix free of vaginal epithelial cells or menstrual blood, and in the absence of primary herpes, trichomoniasis, or candidiasis)
  b. Purulent endocervical discharge; or positive "swab test" (yellow or green color on endocervical swab).
  c. Hypertrophic or edematous cervical ectopy.
  d. Endocervical bleeding induced by gentle swabbing (post coital)

INVESTIGATIONS

- CBC
- Wet smear
- KOH mount
- Gram stain from vaginal swab for gonorrhea
- Culture and medicine sensitivity of gonorrhea and chlamydia
- Ultrasound

TREATMENT

Objective

- Alleviate symptoms
- Treat aggressively to prevent short and long term complications
- Identify and treat the partner and halt further transmission of infection

Pharmacologic

First line

- **Doxycycline**, 100mg P.O., BID for 7 days

Alternatives

- **Erythromycin base**, 500mg P.O., QID for 7 days

OR

- **Azithromycin,** 1.0gm P.O., single dose

○ *Note:* If Gonococcal infection is likely on clinical or epidemiological grounds, proceed treatment with a single dose gonorrhea regimen.

SEX PARTNERS

- All current sex partners should receive full STD evaluation. It is probably most important to evaluate those partners within the past 30 days of diagnosis or onset of symptoms.
- If Non-Gonococcal Urethritis (NGU) or gonorrhea present; treat accordingly.
- If no urethritis is documented in the partners, it is generally safe to defer treatment pending results of tests for gonorrhea and Chlamydia. However, empiric therapy at the time of initial examination may be indicated if follow-up cannot be assured.

22.2.14.3 TRICHOMONAL VAGINITIS

BRIEF DESCRIPTION

- Trichomoniasis is a parasitic infection caused by Trichomonas vaginalis.
- Trichocomonal vaginitis is characterized by the development of profuse, purulent malodorous vaginal discharge (occasionally foamy).
- Cervical petechiae are commonly seen ("strawberry cervix").
- External dysuria and genital irritation are sometimes present.
- As in BV, the vaginal PH in trichomoniasis is generally above 4.5.
- Trichomonas vaginalis may be linked to adverse pregnancy outcomes such as PROM, premature birth, and low birth weight.

CLINICAL FEATURES

- Frothy, greenish and profuse vaginal discharge associated with itching.

INVESTIGATIONS

- Demonstration of motile trichomonads on saline wet mount of vaginal exudates

TREATMENT

Objectives

- Alleviate symptoms.
- Prevent adverse pregnancy outcomes including PROM, premature labour, low birth weight.
- Halt further transmission of the infection by identifying and treating the partner/s.

First line

- Metronidazole, 500mg P.O., BID for 7 days OR 2gm P.O., single dose

Alternative

- Tinidazole, 2gm P.O., stat

In Pregnancy

- **Metronidazole**, 2gm P.O., single dose regimen.
- Advice on abstinence from sexual intercourse until symptoms improve and partner(s) is treated.
- Avoid alcohol during treatment with oral metronidazole and for 24 hours thereafter, due to possible reaction.
- Treatment failure (persistence or recurrence despite sexual abstention, or after intercourse only with a treated partner), metronidazole 500mg P.O bid for 7 days.
- Repeated treatment failure: metronidazole 2.0gm P.O. QD for 3 to 5 days.
- Metronidazole gel is not effective for the treatment of T-vaginalis.
- Consider metronidazole resistance if patient is persistently infested after multiple treatment courses.
- Tinidazole appears to be effective against metronidazole resistant T. Vaginalis: dose is 2 gm once P.O

SEX PARTNERS

- Routine examination for sexually transmitted disease is required.
- Metronidazole 2.0 gm P.O, single dose for all partners.
- Abstain from sexual contact until 7 days after therapy is initiated.

22.2.14.4 VULVO-VAGINAL CANDIDIASIS

BRIEF DESCRIPTION

- Vulvo vaginal candidiasis is a common cause of pruritic vaginal discharge which is commonly caused by one of the 3 species of candida called *Candida albicans*. Although other species are incriminated rarely

CLINICAL FEATURES

- The main manifestations include pruritus vulvae, whitish curd like vaginal discharge, vulvar irritation, dyspareunia, and splash (external) dysuria.

Investigations

- KOH test, to see fungal hyphae, Culture

TREATMENT

Objective

- Alleviate symptoms.
- Identify the underlying cause and manage accordingly including diabetes mellitus, excessive use of board spectrum antibiotics, other causes that can jeopardize the immune status of the patient

Non pharmacologic

- Avoid frequent douching using detergents

Pharmacologic

First line

- **Nystatin**, 100,000 IU per vaginum, QD for 14 days

Alternative

- **Clotrimazole,** 100mg BID to be inserted in the vagina for three days OR 200 mg/day for 03 days. OR 100mg/day for 6 days OR 1% cream 5gm 10-14 days.

OR

- **Miconazole,** 200mg/day to be inserted in the vagina for three days OR 100mg/day for 7 days.

OR

- **Miconazole** 2% cream 5gm intra-vaginal for 7 days.

RECURRENT VULVO-VAGINAL CANDIDIASIS

- Usually associated with underlying immunecompromising state (Diabetes, HIV, Chemotherapy, age etc…)

First line

- Ketoconazole, 400mg /day OR 200 mg BID for 5-10 days. Then 100 mg / day for 6 months as prophylaxis.

Alternative

- The optimal therapy for recurrent vulvovaginal candidiasis in nonpregnant women consists of initial induction therapy with **fluconazole 150** mg every 72 hours for three doses, followed by maintenance fluconazole therapy once per week for six months

SEX PARTNERS

- Examination and treatment of the partner usually is not necessary.
- However, if the partner has penile candidiasis or there is recurrent infection, treatment with an imidazole cream (e.g, miconazole, clotrimazole) may be indicated.

22.2.14.5 ABORTION

BRIEF DESCRIPTION

- Abortion is defined as the initiation or expulsion of the fetus and other products of conception before the 28th week of pregnancy.
- It may be spontaneous (threatened, inevitable, incomplete, complete or missed) or induced.

CAUSES

- Infections e.g. malaria, HIV, UTI, bacterial vaginosis etc.
- Foetal abnormalities
- Incompetent cervix and other congenital anomalies of the uterus
- Chronic illness e.g. diabetes, thyroid disorders, HIV etc.
- Intentional interference with the pregnancy with medications or instrumentation
- Trauma

THREATENED ABORTION

- This is bleeding from the uterus before 28 weeks of gestation without cervical dilatation.

CLINICAL FEATURES

- This variety of abortion usually manifests with scanty to moderate painless vaginal bleeding without cervical dilatation and effacement.
- There may be mild discomfort. Usually, the uterine size corresponds with the stated gestational age.

INVESTIGATIONS

- CBC
- Blood film for malaria and other hemoparasites
- VDRL
- FBS
- HIV test
- Ultrasound scan (confirms viable fetus in utero with closed cervix)

TREATMENT

Objectives

- Maintain a viable pregnancy to term if possible

Non pharmacologic

- Explain the condition to the patient
- Strict bed rest at home or hospital
- Abstain from sexual intercourse
- Report if bleeding or pain increases

Pharmacologic

- In case of early pregnancy (before 9 weeks) there is a place for progesterone 10 mg po/Im for at least 10 days.

- This is to support the luteal phase until the placenta function takes over the production of progesterone

INEVITABLE ABORTION

- Inevitable abortion is bleeding from the uterus before 28 weeks of gestation leading to cervical dilatation with the membranes bulging or leakage of fluid.

CLINICAL FEATURES

- There is lower abdominal pain associated with heavy bleeding, cervical dilatation and effacement. There may also be painless loss of amniotic fluid.
- If the bleeding continues for more than one week, it can be considered as inevitable abortion, even if the cervix is closed.
- The uterine size is compatible with the gestational age.
- Depending on the amount of blood loss, there may be signs of shock (pallor, collapsed peripheral vessels, rising pulse with reducing volume, falling BP and cold clammy skin).

INVESTIGATIONS

- CBC
- Blood grouping and cross matching
- Ultrasound scan to see the viability of the fetus, for assessment the cervix, to also look for possible cause and amniotic fluid volume

TREATMENT

Objectives

- Resuscitate patient
- Relieve pain
- Facilitate conditions that the process of abortion to be accomplished in aseptic condition within short period of time.
- Evacuate the retained products of conception from the uterus.

- Identify cause of abortion if possible.
- Prevent infection with antibiotic prophylaxis.
- Provide Anti D injection (50-300 mcg IM stat) in case of an RH negative status

Non pharmacologic

- Keep the patient NPO
- Blood transfusion, if required, Use uterotonics such as ergometrin or misoprostol in case of intractable bleeding

Pharmacologic

- **If** the **uterine size larger than 14 weeks, IV fluids** as necessary.
- **Pethidine**, IM, 75-100mg stat. Followed by 50-100mg 8 hourly promethazine hydrochloride, IM, 25mg stat
- **Oxytocin**, IV, 10-20 units/litre of Normal saline

OR

- **Misoprostol**, per vaginum or rectum, 600-800micrograms, two doses 4 hours apart
- **Post abortion antibiotic prophylaxis** is also recommended (Doxycline 100 mg po BID for 7 days)
- Provide comprehensive abortion care.

Incomplete abortion

- In this clinical scenario part of the conceptus material is expelled and some is remaining in the uterine cavity or cervical canal.

Clinical features

- The patient may complain of the passage of large clots and/or the fetus and some products of conceptus material per vaginum.
- Depending on the extent of bleeding patient may manifest with shock (collapsed peripheral vessels, fast pulse, falling BP and cold clammy skin).

- Usually the uterine size is smaller than the stated gestational age.
- Cervix is dilated and part of the conception material may be in the cervical canal.

Investigations

- CBC
- Blood grouping and cross matching
- Ultrasound scan
- RFT, LFT
- Erect plain film of the abdomen, if perforation is suspected (when MVA is

Treatment

Objectives

- Resuscitate patient
- Evacuate the retained products of conception from the uterus
- Prevent infection with antibiotic prophylaxis
- Identify the cause of abortion, if possible
- Prevent risk of Rh isoimmunization

Non pharmacologic

- Digital curettage during the time of vaginal examination to decrease blood loss.
- Arrange for surgical evacuation of the retained products of conception by manual vacuum aspiration (MVA) or metallic evacuation and curettage (E&C).
- Abstain from sexual intercourse for at least 2 weeks.
- Counseling and psychological support of the patient.
- Blood transfusion when needed

Pharmacologic

- **IV fluids** as necessary.
- **Ergometrine**, IM/IV,0.2-0.4mg stat
- **Oxytocin**, IV, 20 units into 1 Lt of N/S and infuse at 30-60 drops per minute

OR

- **Misoprostol**, rectal, 600-800micrograms two doses 4hours apart. If the woman is RH negative and husband is RH positive: Anti D Rh Immune Globulin 250-300 Units (150mg), IM, stat within 72 hours.
- **Amoxicillin**, 1gm PO 6 hourly for 7days

Complete Abortion

- Cessation or reduction of vaginal bleeding following heavy bleeding with passage of clots and/or the fetus and placenta.

Clinical features

- Usually the patient has no pain.
- The uterus is smaller than the gestational age.
- The cervix is closed and firm.

Investigations

- CBC
- Blood grouping and cross matching
- Ultrasound scan: to confirm empty uterine cavity

Treatment

Objectives

- Assess for and manage anaemia if present.
- Investigate for the cause of abortion if possible

Non pharmacologic

- Counseling and psychological support of the mother

Pharmacologic

- Resuscitate patient if necessary
- Treat anaemia if present
- Follow up

22.2.15 SEPTIC ABORTION

BRIEF DESCRIPTION

- This is a life-threatening complication of abortion.
- Most often the patient gives history of interference with pregnancy under septic technique or incomplete abortion which stayed for some time without being evacuated.
- If not managed appropriately, this may lead to further complications such as septic shock, uterine damage, peritonitis, haemorrhage, disseminated intravascular coagulation (DIC), acute renal failure, adult respiratory distress syndrome, tetanus or gas gangrene.

CLINICAL FEATURES

- Severe lower abdominal pain, fever, vomiting, headache, offensive and bloody vaginal discharge, tachycardia, sign of peritonitis.
- If conditions worsen, patient may manifest with septic shock.

INVESTIGATIONS

- CBC
- Coagulation profile
- Blood grouping and cross matching
- Blood culture and sensitivity
- Urine culture and sensitivity
- Endo-cervical swab for culture and sensitivity

- Blood urea and electrolytes
- Chest and abdominal X-ray (to exclude foreign body, gas under the diaphragm suggesting uterine perforation)
- Abdomino-pelvic ultrasonography (for intra-abdominal and pelvic abscesses, peritonitis and gas in the pelvis)

TREATMENT

Objectives

- Resuscitate patient
- Treat infection
- Evacuate uterus and prevent further infection or organ damage
- Provide counseling

Non pharmacologic

- Evacuate the retained products of conception. Careful evacuation of the uterus must be done as risk of uterine perforation is high.
- Do gentle digital curettage followed by the instrumental curettage under general anaesthesia within 6 hours of initiation of antibiotic therapy. Extreme care is needed in order not to perforate the uterus (if it has not been perforated already).
- If there is sign of peritonitis or uterine perforation, laparotomy may be required.
- Psychological support and family planning counseling.
- Blood transfusion when required

PHARMACOLOGIC

- **IV fluids as necessary.**
- If the gestational age is above 14 weeks and the fetus is not aborted yet, **Oxytocin**, IV, 20units in 1Lt of N/S to run 50-60drops/min
- **Ampicillin**, IV,1-2 g 6 hourly for 24-72 hours

PLUS

- **Gentamicin**, IV, 80 mg 8 hourly for 24-72 hours

PLUS

- **Metronidazole**, IV,500 mg 8 hourly for 24-72 hours
- **Switch** over from IV to oral therapy when appropriate. Continue with gentamicin, IM or IV, 80 mg for at least 7 days. (The culture and sensitivity test results will direct the antibiotic therapy)
- **Pethidine**, IM, 100 mg 4-6 hourly with Promethazine, IM, 25 mg 8-12 hourly
- **Tetanus prophylaxis**, if there is interference with pregnancy under septic condition.

MISSED ABORTION

- **This** refers to foetal death in-utero before 28 weeks gestation which does not show any sign of expulsion.

CLINICAL FEATURES

- There is reversal of the symptoms of pregnancy with recurrent bloody vaginal discharge.
- The mother fails to perceive the foetal movements (if quickening has already occurred).
- The uterus is smaller than the stated gestational age. The foetal heart beat is absent.

Investigations

- CBC
- Blood grouping and cross matching,
- Blood film for malaria parasites if the clinical features suggest acute febrile illness
- Blood clotting profile

- Pregnancy test
- Ultrasound scan
- Fasting Blood Sugar
- VDRL

TREATMENT

Objectives

- Prepare the patient for uterine evacuation
- Ensure safe uterine evacuation
- Ensure there is no DIC before attempting to evacuate the uterus
- Establish cause of foetal death if possible

Non pharmacologic

- First trimester (<12 weeks): Evacuation of the uterus can be accomplished by suction curettage (manual or with machine) or using the metallic curettes (E&C).
- Hysterotomy may be indicated where induction fails or is contraindicated.
- Blood transfusion when the need arises

Pharmacologic

- **IV fluids** as necessary
- **Misoprostol**, oral or vaginal, 400micrograms stat, at least 3 hours prior to suction curettage. This will facilitate curettage and prevent damage to the cervix by metallic dilatation. Misoprostol can also be used to both ripen the cervix and facilitate evacuation of the uterus. If there is previous uterine scar decrease the dose by half and use mechanical means such as cervical catheter and laminaria dilators if available.

IF 12–24-WEEK GESTATION:

- **Misoprostol**, 200micrograms, vaginal, 12 hourly until expulsion or 400micrograms, oral, 4 hourly until expulsion.

IF 4–12-WEEK GESTATION:

- **Misoprostol**, 800micrograms, vaginal or sublingual, every 24 hours for two days
- **Intrauterine foetal death (>24 weeks) with previous caesarean section consider;**
    - **13-17 weeks**: 200microgram 6hourly
    - **18-26 weeks:** 100microgram 6hourly
    - **27-42 weeks:** 25-50microgram 4hourly
    - **Induction of labour (live fetus >24 weeks)**: 25-50microgram vaginally 4 hourly

INDUCED ABORTION

Brief description

- This refers to the deliberate termination of pregnancy.
- Termination of pregnancy is requested for and done for reasons permissible by law either through a surgical procedure or by pharmacological means.
- The Ethiopian law permits to terminate pregnancy under the following conditions:
    - In case of rape, defilement or incest
    - Threat to physical and mental health of the mother
    - Presence of foetal abnormality
    - Mental retardation of the mother
    - Minors aged under 18
    - Any medical condition that endangers the life of the mother if pregnancy continues

Treatment

Objectives

- Ensure that legal requirements for termination are met
- Ensure the termination is performed safely
- Provide family planning counseling after the procedure
    - If pregnancy is following rape, management should follow the guide on providing care for survivors of sexual assault

Non pharmacologic

- **Pre-abortion Counseling**
    - Advise on the other possible options before deciding on termination.
    - Explore the reasons for the abortion request to ensure that it meets the legal and medical requirements.
    - Provide information of other care options and on the available methods of abortion.
- **4-12 weeks gestation**: Manual Vacuum Aspiration; Dilatation and curettage
- **12 weeks gestation:** Cervical ripening with misoprostol or prostaglanding E2, followed by dilatation and evacuation/ extraction

Pharmacologic

- **4-12 weeks of gestation**:
    - **Mifepristone**, 200mg P.O., stat followed by after 24 hours misoprostol 800 microgram, then the same dose 4 hours.
- **12-24 weeks gestation:**
    - **Misoprostol**, 400 micrograms PO 4 hourly until expulsion

OR

- **Mifepristone,** 200mg P.O., stat, followed by **Misoprostol** 200microgram P.O., after 24 hours

22.3 GYNECOLOGICAL DISORDERS

22.3.1 ABNORMAL UTERINE BLEEDING (AUB)

BRIEF DESCRIPTION

- Menstruation is considered normal:
    - If the cycle comes every 21 to 35 days,
    - The duration of bleeding is 1 to 7 days
    - The amount is less than 80ml and
    - It is not associated with any pain.
- Anything other than this is considered abnormal.
- Abnormal uterine bleeding includes dysfunctional uterine bleeding (DUB), i.e., uterine bleeding with no organic cause and bleeding from structural causes.
- Dysfunctional bleeding can be ovulatory or anovulatory.
- The Anovulatory variety is the commonest type (greater than 80%), usually occurring in post- menarche and premenopausal periods.
- It is characteristically acyclic, unpredictable as to the onset of bleeding, and variable in the duration and amount of bleeding.
- Ovulatory DUB is usually associated with premenstrual symptoms such as breast tenderness, dysmenorrhea, and weight gain and regular periodicity but heavy in amount (heavy menstrual bleeding).
- Usually, it is caused by organic lesions, although a dysfunction of the corpus luteum or atrophic endometrium may be the causes.
- Structural causes include fibroids, polyps, endometrial carcinoma, and pregnancy complications.

DYSFUNCTIONAL UTERINE BLEEDING (DUB)

CAUSES

- Hypothalamic dysfunction (physiologic)
- Premature ovarian failure
- Polycystic Ovarian Syndrome
- Hypo or Hyper-thyriodism
- Coagulation disorders

CLINICAL FEATURES

- The diagnosis is made by excluding all other obvious causes of abnormal uterine bleedings.

INVESTIGATIONS

- CBC, coagulation profile, pregnancy test, ultrasound, Saline Infusion Sonography, hysterosalpingography, endometrial sample
- TSH, T3, T 4
- Differentiate between ovulatory and anovulatory causes : serum progesterone on day , endometrial biopsy, Basal Body Temperature (BBT).
- If anovulatory: Prolactin, FSH, LH, free testosterone, 17-hydroxprogesterone
- For advanced chronic diseases: LFT and RFT

ANOVULATORY DUB TREATMENT

The treatment depends on the age of the patient, her desire for contraception or fertility, and the severity and chronicity of the bleeding.

Objectives

- Control active bleeding
- Prevent recurrences, restoration of normal cycle
- Induce ovulation in patients desiring to conceive.

Non pharmacologic

If the haemoglobin level is low (less than 7gm/dl), transfuse 2 units of blood.

Pharmacologic

Control of active bleeding:

First line

- **Norethisterone**, 5mg QID P.O. for 2-3 days followed by 5mg P.O. QD for ten days

with or without

- **Medoxyprogesterone,** 10-25mg QID, P.O. until bleeding stops

Alternative

- **High dose of combined oral contraceptive pill** (COP) 1tablet QID, for 4 days, followed by 1tablet, TID for 3days, then followed 1tab BID for 2 days until the bleeding is controlled and then the standard dose of the COP one tablet/day for 21 days.
- If there is vomiting while taking the high dose COP, **promethazine** 25mg, PO or IM should be given.

Note: If bleeding failed to stop despite high dose of Combined oral contraceptive pill, Dilation and Curettage may be required.

RESTORATION OF THE CYCLE

- **Combined oral contraceptive pills** 1 tablet/day for 21 days for 3-4 consecutive months.
- **Norethisterone** 5mg/day from day 14-24 each month for three months.

If fertility is desired, ovulation induction using clomiphene citrate is one modality of treatment.

OVULATORY DUB

- This is commonly diagnosed by the presence of clinical evidence of ovulation and is confirmed by hormone analysis and/or endometrial biopsy, Basal Body Temperature (BBT) and stretching of cervical mucus.

- It is usually due to follicular or luteal phase defect.

Treatment

Objectives

- Identify the underlying cause
- Prevent recurrence

Non pharmacologic

If there is any clinical suspicion of endometrial pathology, either of the following measures is appropriate:

- Manual (electrical) Vacuum Aspiration or using pippet for endometrial biopsy
- Dilatation & curettage
- Endometrial ablation
- Hysterectomy

Pharmacologic: Before embarking on treatment, organic causes should be ruled out beyond shadow of doubt.

First line

- Prostaglandin inhibitors or NSAID medicines are given few days before the bleeding starts and the first three days of the bleeding.
  - ○ **Ibuprofen,** 400mg 3 times /day or **Indomethacin**, 25-50mg P.O., TID

Alternative

  - ○ **Danazol**, 200-400mg P.O., daily for 12 weeks

- **Structural causes:** The treatment depends on the underlying cause.

Note: Minor variations of normal bleeding pattern may not require evaluation, particularly in the first 2 years of menarche

23.3.2 DYSMENORRHOEA

BRIEF DISCUSSION

- Dysmenorrhoea is excessive pain during menses.
- It occurs in about 50% of menstruating women.
- It may be primary or secondary.
- Primary dysmenorrhoea is believed to be due to increased endometrial prostaglandin production, whereas
- Secondary dysmenorhoea is due to outflow obstruction, pelvic tumours, infections, endometriosis etc.
- Dysmenorrhea in the first few years following menarche is usually primary but the secondary characteristically occurs many years after menarche.

CLINICAL FEATURES

- The pain of primary dysmenorrheal usually begins a few hours prior to or just after the onset of menstrual flow and may last as long as 48-72 hours.
- Thorough pelvic assessment is important to rule out organic causes.

INVESTIGATIONS

- CBC, vaginal smear, ultrasound

TREATMENT

Objectives

- Alleviate pain
- Treat underlying cause

Primary dysmenorrhea

Non pharmacologic:

- Reassurance

Pharmacologic

First line

- **Prostaglandin inhibitors (NSAID)**: **Ibuprofen**, 400 mg, P.O., TID

OR

- **Mefenamic acid**, 500mg, P.O, TID.

Note: The medicines have to be administered prior to the onset of menses or at the onset of pain every 6 to 8 hours for the first few days of menses. This modality of treatment should continue for 4-6 months before declaring treatment failure.

Alternative

Monophasic Combined oral contraceptive pills; if contraception is also needed

SECONDARY DYSMENORRHEA

- It is cyclic pain in association with underlying pelvic pathology.
- The pain often begins 1-2 weeks prior to the onset of menses and persists until a few days after cessation of bleeding.

Treatment

Unlike primary dysmenorrhea, Non-steroidal anti-inflammatory medicines (NSAID) and oral contraceptive have limited roles. The underlying cause should be treated. The most common cause is endometriosis.

23.3.3 INFERTILITY (MALE AND FEMALE)

- Infertility is defined as one year of unprotected intercourse without pregnancy.
- It could be primary or secondary.
- The major causes of infertility in female could be fallopian tube occlusion or anovulation.

- In males, it could be pre-testicular, testicular or post-testicular affecting the semen quality in terms of volume, sperm count, morphology, concentration, and motility.
- In sub-Saharan Africa it is estimated that 11-20% couples have difficulty conceiving.
- The effect may be amplified for those living in the infertility belt of Africa which stretches from Tanzania in the east to Gabon in the west.

CAUSES

- Infection:
  - o STI (chlamydial, gonorrhea, syphilis etc.)
  - o Infectious and parasitic diseases: mumps, TB, schistosomiasis
  - o Post-partum/abortal
- Exposure to toxic substances: arsenic, aflatoxins, pesticides, caffeine, tobacco, alcohol, heat
- Anovulation: the main cause being polycystic ovarian syndrome (PCOS) in 75%of cases
- Surgery, trauma

CLINICAL FEATURES

- History of STD, features of endocrinopathies,
- History of contraception usage,
- Surgical history (ovarian cyst, appendectomy, pelvic abscess, ochidopexy, repair of inguinal hernia),
- Medicine intake, diet (smoking, excessive alcohol and caffeine consumption),
- Galactorrhea,
- Menstrual pattern, dysmenorrea,
- Current illness,

- Occupation (male)

Investigations

- CBC
- FBS
- Vaginal smear
- Hormone profile:
  - To evaluate ovarian reserve (serum FSH and LH in 1-3rd day of the menstrual cycle),
  - For ovulation evaluation: Serum progesterone, 7 days before the expected menses
  - If menstruation is irregular: TSH, T3, T4, Testosterone, DHEA, DHEAS, prolactin
- Hysterosalpingography (HSG)
- Ultrasound: ovarian volume, counting ovarian follicles
- Laparoscopy: to look for endometriosis and tubal patency
- For male: Sperm analysis, vasography, testicular biopsy, trans-rectal ultrasound, hormone assay (FSH, LH, prolactin, thyroid function tests, testosterone), post-ejaculatory urine examination for male with an ejaculatory volume < 1ml.

Treatment

Objectives

- Identify the exact cause of infertility and manage it accordingly Give couples a realistic prognosis of treatment.
- Provide information, support and counseling to the couples to cope with the stress of treatment and possible failure

Non pharmacologic

- Overweight or underweight should be normalized

- Stress should be alleviated.
- Avoid smoking, excessive alcohol and caffeine consumption

Pharmacologic

Female

- **Clomiphene citrate,** starting dose 50mg/day PO for five days starting from the 5th day of the menstrual cycle, and if no ovulation increases the dosage by 50mg/day up to 200mg/day over three to four treatment cycles.
- If possible, check mid-luteal phase progesterone in each cycle for ovulation
- **HCG** 5000-10,000IU IM 5days after the last clomiphene tablets may enhance ovulation

OR

- Metformin: Recently metformin has been used to induce ovulation, If the cause of anovulation is PCOS Starting dose: 500mg/day for one week, if tolerated, double the dose for another one week, then
- 1500mg daily, gradually increase the dose to reach maximum, 2500mg/day.
- The treatment can continue for six months.

Note: There is no need of increasing the dose if the menstrual cycle becomes regular.

OR

- **Clomiphene and metformin combined:** Women with PCOS, 90% will ovulate

OR

- **Tamoxifen**, P.O., 20-40mg/day, from day 3 of the menstrual cycle for 5 day

OR

- **Gonadotrophins:** Human menopausal gonadotrophins (HMG), (for women resistant to above mentioned medicines), IM, 75IUday for 14days in step-up manner.

Male:

Non pharmacologic

- Avoid smoking, excessive alcohol and caffeine consumption
- Avoid exposure to environmental toxic substances (arsenics, aflatoxins) and heat
- Surgical: Varicocele repair, vassal reconstructions, Intracytoplasmic sperm injection (ICSI)

Pharmacologic

- None except in retrograde ejaculation, sympathomimetics such as imipramine and pseudoephedrine, can be tried.

23.3.4 MENOPAUSE AND PERIMENOPAUSAL HORMONE SYNDROME

BRIEF DESCRIPTION

- Menopause refers to the point in time when permanent cessation of menstruation occurs usually due to loss of ovarian function.
- A woman is considered to be menopausal if there is no menstruation for a period of at least 12 months in the absence of pregnancy or lactation.
- Menopause is associated with physical, emotional and psychological upheaval of varying intensity in the affected individual.
- Sixty percent of menopausal women may be asymptomatic.
- To alleviate symptoms and prevent osteoporosis and other cardiovascular problems, Hormone Replacement Therapy (HRT) used to be recommended for every post-menopausal woman.

- However, following the release of Women Health Initiative (WHI) study result in 2002, many societies and health organizations consider HRT as dangerous and the routine use of HRT was disrupted.
- Recently, several high ranking Obs/Gyn specialists and the International Menopausal Society (IMS) re-affirmed and re-legitimized the use of HRT for at least 5years in healthy post-menopausal women less than 60 years of age.

CAUSES

- Natural onset due to the age of the individual
- Due to surgical removal of the ovaries (bilateral oophorectomy)
- Pelvic irradiation
- Premature ovarian failure due infection and other causes
- Pituitary damage from primary post-partum haemorrhage (PPH) (Sheehan's syndrome
- Cytotoxic (anticancer) therapy

CLINICAL FEATURES

- Hot flushes (heat or burning in the face, neck and chest with resultant sweating).
- The flushes may be associated with palpitations, faintness, dizziness, fatigue, weakness, emotional and psychological problems which include: mood changes, depression, anxiety, nervousness, irritability, loss of libido.
- Atrophic changes in the genital tract may give rise to the following: increased frequency of micturition and dysuria, vaginal dryness and dyspareunia.

INVESTIGATIONS

- Hormone tests if available (serum LH, FSH, estradiol).
- Routine investigations e.g. CBC, blood glucose, lipid profile.
- X-ray to evaluate bone density.

- Investigation to exclude pregnancy

TREATMENT

Objectives

- Control symptoms e.g. severe hot flushes, atrophic vaginitis and recurrent cystitis.
- Prevent osteoporosis especially in individuals with premature menopause.
- Prevent cardiovascular morbidity and mortality

Non pharmacologic

- Counseling and reassurance.
- Encourage active lifestyles, exercise and regular physical checkups for common medical problems.
- Avoid hot weather conditions
- Light clothing, cold shower
- Balanced diet

Pharmacologic

In women with intact uterus:

- HRT can be given as sequentially opposed or continuous combined preparations.
- The continuous preparations have the advantage of less breakthrough bleeding, but should only be commenced once the woman has been stable on sequentially opposed therapy for a year.
- Treatment should last 5 years but should be reviewed annually.

SEQUENTIALLY OPPOSED HRT

- **Conjugated equine oestrogen**, 0.3-0.625mg P.O., daily for 21 days

OR

- **Medroxyprogesterone acetate**, MPA 5-10mg P.O., daily

OR

- **Norethisterone acetate** oral 1mg daily from day 11-21 followed by no therapy from day 22-28

OR

- **Estradiol valerate**, oral, 1-2mg daily for 11days

PLUS

- **MPA**, 10mg P.O., daily from day 11-21 followed by no therapy from day 22-28

Continuous combined therapy

First line

- **Conjugated equine oestrogen**, 0.3-0.625mg P.O.,

PLUS

- **MPA**, 2.5-5mg P.O., daily

Alternative

- **Estradiol valerate**, 0.5-1mg P.O.,

PLUS

- **Norethisterone acetate**, 0.5-1mg P.O., daily

IN WOMEN WITH PREVIOUS HYSTERECTOMY:

- **Conjugated oestrogens** 0.625 microgram daily**.**
- Women with intact uteruses should never be given oestrogen alone.

Note: Start at the lowest dose of HRT to alleviate symptoms. The need to continue HRT should be reviewed annually. If HRT is continued, it should be gradually tapered because abrupt discontinuation of oestrogen may cause recurrence menopausal symptoms. A mammogram should be done once every two years. Abnormal vaginal bleeding requires evaluation by a specialist to exclude endometrial cancers.

REFERRAL

- Refer cases with osteoporosis or severe unremitting symptoms.
- Women with premature ovarian failure
- Women with post-menopausal vaginal bleeding

23.3.5 CARCINOMA OF THE CERVIX

BRIEF DESCRIPTION

- Carcinoma of the cervix is the commonest form of female genital cancer in the developing countries.
- Though common, it is preventable and curable if detected early.
- In developed countries, the incidence of this disease has fallen considerably owing to regular screening procedures using the Pap smear.
- In the absence of an effective screening system in Ethiopia, most cases seek clinical care very late and thus the only modality of treatment left for these patients is radiation.

CAUSES

- Human papilloma virus, the high oncogenic types are implicated in the causation of the disease.
- There are more than 18 high oncogenic types.
- The other associated factors include:
    - Associated risk factors
    - Sexual promiscuity
    - First coitus at early age, multiple child births
    - Infections with Herpes Simplex Hominis type II, HIV
    - Smoking

  - Low socio-economic status
  - Family history
  - Immunosuppression

CLINICAL FEATURES

- Some are asymptomatic in the early stage of the disease (diagnosed on routine screening or assessment during antenatal care, family planning etc.)
- Commonly patients present with abnormal vaginal bleeding after sexual intercourse, post-menopausal bleeding, and increased vaginal discharge.
- In early cases there will be erosion of cervix or changes of chronic cervicitis but in advanced cases ulcerative or fungating cervical lesion is observed on speculum examination.

INVESTIGATIONS

- Cervical biopsy
- CBC
- Renal function test
- Serum uric acid
- Chest radiograph
- Intravenous urography
- CT Scan and or Magnetic Resonance Imaging (to detect aortic nodes and metastases to the lungs and liver)
- Examination Under Anaesthesia for clinical staging

PREVENTION

- Vaccine: Recently, a quadrivalent vaccine against 16,18,6 and 11(Gardasil) from MSD and bivalent vaccine against 16 and 18 (Cervarix) from GSK has been developed and made available to the market.
- These vaccines are 70-80% effective in preventive cervical cancer.

Screening:

- Pap smear, VIA, VILI and colposcopy

Treatment

Objectives

- Treat central tumor
- Treat areas of tumor spread with the aim of eradicating the disease
- Alleviate symptoms in advanced cases

Non pharmacologic

The treatment modalities for carcinoma of the cervix are:

- Surgery, the main stay treatment
- Radiotherapy: as treatment or palliation to arrest vaginal bleeding or alleviate pain
- A combination of surgery and radiotherapy
- Adequate nutrition
- Correction of anaemia
- For advanced terminal cases: provide emotional and psychological support

Early disease

Stage IA1

- Depth of stromal invasive less than 3mm with horizontal expansion of 7mm
- Simple conization of the cervix may be enough if the patient desires fertility and provided surgical margins are free of cancer or extra fascial hysterectomy if childbearing has been completed.
- If there is lympho-vascular invasion more aggressive treatment is appropriate.

Stage IA2

- Depth of invasion 3-5mm with 7mm horizontal spread
- Requires extensive surgery (modified radical hysterectomy with pelvic lymphadenectomy).

Overt disease (Stage IB and IIA)

- Radical hysterectomy with pelvic and para-aortic lymphadenectomy.

Advanced disease (Stage IIB to IV)

- The modality of treatment is radiotherapy, with or without chemotherapy.
- Currently, in USA the standard treatment is to give weekly cisplatin 1mg/kg during radiation therapy.

Pharmacologic

Neoadjuvant chemotherapy

- **Cisplatin**, 1mg/kg, IV, diluted in 1L N/S over 24hours weekly for 3 weeks. If given before surgery or radiation, patient will have better survival rate.

Palliative treatment

- Patients with end-stage cervical cancer may present with different clinical presentations such as pain from bony metastasis, respiratory distress from lung metastasis and renal failure secondary to tumor growth.

Palliative chemotherapy: A combination of cisplatin and paclitaxel has a better response rate

Pain management: Follow the WHO ladder approach

- Start with Non-steroidal anti- inflammatory medicines (NSAIDs) or the newer cyclo-oxygenase-2 (COX-2) inhibitors.
- If the patient fails to respond to these agents, proceed to second line of medicines which are opioids such morphine.

Respiratory distress: **Oxygen support** and withhold toxic medicines

Renal failure: Percutaneous nephrostomies

REFERRAL

- All patients must be referred to a specialist for evaluation and decide on mode of treatment.
- The treatment of carcinoma of the cervix is best done by a specialist who has experience in cancer management.

23.3.6 GESTATIONAL TROPHOBLASTIC DISEASES (GTD)

BRIEF DISCUSSION

- GTD comprises a spectrum of neoplastic conditions in women derived from the placenta.
- The term GTD includes hydatidiform mole (complete mole &partial mole) invasive mole, gestational choriocarcinoma, and placental trophoblastic tumor (PTT)
- Gestational Trophoblastic Neoplasia (GTN) refers specifically to forms with the potential for tissue invasion and metastasis which includes invasive mole, choriocarcinoma, PTT and post molar trophoblastic diseases.
- GTN is recognized today as the most curable gynecologic malignancies.

CLASSES

- Hydatidform mole (Complete mole and Partial mole)
- Invasive mole
- Choriocarcinoma
- Placental Trophoblastic Tumour (PTT)

CLINICAL FEATURES

- The classic presentation includes irregular vaginal bleeding, hyperemesis, execessive uterine enlargement, expulsion of vesicles and failed early pregnancy.
- Rarer presentations include hyperthyroidism, early onset pre-eclampsia or

abdominal distension due to theca lutein cysts.

- Very rarely, women can present with acute respiratory failure or neurological symptoms such as seizures; these are likely to be due to metastatic disease.

INVESTIGATIONS

- Ultrasound: snow-storm appearance is observed in complete mole and in partial mole there will be cystic spaces in the placenta and transverse to antro-posterior diameter of gestational sac is greater than 1.5.
- Serum or urine HCG.
- Histological examination of the tissue removed.
- Thyroid function tests (TSH, T3, T4).
- Coagulation profile (PT,PTT, INR)
- CBC
- Renal function test (urea, creatinine)
- Liver function test
- Blood group and cross-match

TREATMENT

Objective

- Resuscitate and stabilize the patient.
- Early detection of persistent mole and manage appropriately.
- Institute chemotherapy using the FIGO 2000 risk scoring system

Non pharmacologic

- If there is heavy bleeding resuscitate the patient
- Surgical evacuation of the uterus (suction curettage is the preferred method)
- Hysterectomy, if the woman has completed her family. This may eliminate

local invasion but not distant metastasis.

- If there is sign of pulmonary insufficiency: Oxygen and cardiopulmonary support

Pharmacologic

- If there is sign of hyperthyroidism, it is important to administer a beta-adrenergic antagonist before the induction of anesthesia for surgical evacuation because of the risk of precipitated thyroid storm.
- **Proporanolol**, IV, 40mg BID

POST-MOLAR SURVEILLANCE

- After evacuation of the molar tissue or hysterectomy with mole in situ, weekly determinations of βhCG until the results are within normal limit for 3 consecutive weeks, then at monthly intervals for 6 months.
- FIGO criteria for the diagnosis of post-molar GTD
  - Four values or more of hCG documenting plateau (10%of hCG value) over at least 3 weeks: days 1, 7, 14, 21
  - A rise of hCG of 10% or greater for 3 values or longer over at least 2 weeks: days 1, 7, 14
  - The presence of histologic choriocarcinoma
  - Persistence of hCG 6 months after molar evacuation

Risk for post-molar gestational trophoblastic neoplasia

- Increase serum hCG level
- Uterine size larger than the expected by date
- Theca-lutein cysts
- Increasing maternal age

Chemotherapy

- The need for chemotherapy following complete mole is 15% and 0.5% for partial mole.

- Women are assessed before chemotherapy is initiated using the FIGO 2000 risk scoring system.
- Women with score ≤6 are at low risk category and treated with a single agent:
- **Metotrixate**, 1mg.kg IM/P.O. days 1, 3, 5, 7 alternating with Folinic acid 0.1mg/kg days 2, 4,6, 8 (repeated every 14days)
- Women with score ≥7 are at high risk category and treated with multiple agent chemotherapeutic agents that include: (see table 22.2 below)

Table 22.1: EMA-CO regimen for high risk malignant GTD

Day	Agent	Dose and route
1	Etoposide	100mg/m^2 IV infusion over 30minutes
	Methotrexate,	100mg/m^2 IV bolus
	D actinomycin	350mg/m^2 IV bolus
2	Etoposide	100mg/m^2 IV infusion over 30minutes
	D actinomycin	350mg/m^2 IV bolus
	Folinic acid	15mg, Po/IM Q 12hourly 4doses,24 hours after methoterixate bolus
8	Cyclophosphamide	600mg/$m^{2,}$ IV infusion over 30minutes
	Vincristine,	1 mg/m2, IV bolus
15	Begin next cycle	

- Treatment should continue, in all cases, until the hCG level has returned to normal and then for a further six consecutive weeks.

Table: 22.2. FIGO scoring system

FIGO scoring	**0**	**1**	**2**	**3**
Age	<40	>40		
Antecedent pregnancy	Mole	Abortion	Term	
Interval from end index pregnancy to treatment (months)	<4	4-<7	7->13	≥13
Pre-treatment serum hCG	$<10^3$	0^3-$<10^4$	10^4-$<10^5$	$\geq 10^5$
Largest tumour size, including uterus(cm)	<3	3-<5	≥5	
Site of metastasis	Lung	Spleen, Kidneys	Gastrointestinal	Liver, Brain
Number of metastasis	-	1-4	5-8	≥8
Previous failed chemotherapy	-	-	Single	2 or more

Note:

- Histological examination of all failed product of conception is recommended to exclude GTN.
- A urinary pregnancy test should be performed in all cases of persistent or irregular vaginal bleeding after pregnancy events.
- Women who undergo chemotherapy are advised not to conceive for one year after completion of treatment.
- Women with GTD should be advised to use barrier methods of contraception until hCG level normalizes. Once hCG is normalized, Combined oral contraceptive pill can be used.

- IUCD should not be used until hCG levels are normal to reduce the risk of uterine perforation.
- Anti-D prophylaxis: Because of the poor vascularization of the chorionic villi and absence of the anti-D antigen in complete mole, anti-D gammaglobulin is not required after evacuation of complete mole but should be given following partial mole.
- Women who receive chemotherapy for GTN are likely to have an earlier menopause.

23.3.7 HORMONAL CONTRACEPTIVES

- Contraceptives include different kinds of methods used to prevent the occurrence of pregnancy.
- The variety of contraceptive methods includes, natural methods, barrier methods, intrauterine contraceptive devices, hormonal and permanent surgical methods.
- Hormonal contraceptives are one of the most effective methods that are prescribed to a client based on informed choice.

COMBINED ORAL CONTRACEPTIVES (COC)

- A group of contraceptive medications composed of synthetic oestrogens and progesterone in different doses; 20mcg, 30mcg or 50mcg of oestrogen and 0.15-1mg of progesterone in each tablet.
- They act primarily by inhibiting ovulation, and also by making the cervical mucus less favorable to sperm penetration and rendering the endometrium more atrophic.

First line

- **Levonorgesterol+ethnylestradiol** and iron, in starting from the first day of menses.

Alternative

- **Norethindrone + Ethnylestradiol**, 0.5mg + 0.035mg /day starting from the first day of menses

OR

- **Norethindrone + Mestranol**, 1mg + 0.05mg /day starting from the first day of menses

Progesterone Only Contraceptives (POP)

- This is indicated whenever there is contraindication for oestrogen as in lactating mothers, Diabetics and Hypertensive patients.
- However, it is less effective compared with COC.

Orals

- **Lynestrenol**, 0.5 mg/day

Injectables

- **Medroxyprogesterone acetate**, 150 mg deep IM injection within the first 5 days of the cycle to be repeated every three months.

Implants

Levonorgesterel in six silastic capsules implanted in the left upper arm under local anesthesia, effective up to five years.

Emergency contraception (EC)

- Contraception aimed at preventing pregnancy after unplanned sexual exposure in a woman who is not on regular contraception. EC cannot be used as a regular method of contraception.

First line

- **Levonorgesterol**, two 0.75mg tablets to be taken 12 hours apart within 72 hours unplanned sexual exposure

OR

- **Combined oral contraceptive pill (COC) with 50 microgram of oestrogen**, 2 tabs BID within 72hours of unplanned sexual exposure for 2doses.

OR

- **Combined oral contraceptive pill (COC) with 35microgram of oestrogen**, 4 tabs BID within 72 hours unplanned sexual exposure for two doses

  Alternative

- **IUD:** This would be effective if inserted within five days of unplanned exposure, after ruling out the existence of infection.

23.3.8 SEXUAL ASSAULT

- Sexual assault is defined as any sexual act performed on another person without consent.
- Physician evaluating the victim of sexual assault should aim at providing adequate medical care and collect evidence. Rape is the most common reported sexual assault.

INVESTIGATIONS

- History and physical examination
- Identification of spermatozoa from specimen over the genitalia or high vaginal swab.
- Tests for chlamydia and gonorrhea.
- Wet mount for trichomonas.
- The wet mount can also be examined for evidence of bacterial vaginosis and candidiasis.
- Serum testing for HIV infection, hepatitis, and syphilis.
- Pregnancy testing should be done for women of childbearing age

TREATMENT

Objectives

- Medical or surgical treatment of acute injury.
- Screen for STI, HIV, Hepatitis virus B infection and pregnancy at initial visit, repeat screening for HIV, HbsAg at three and six months.

- Prevention of STI.
- Prevention of pregnancy
- Rehabilitation
- Medical recording should be meticulous and management approach should be multidisciplinary

Non pharmacologic

- Rehabilitation: counseling and psychological support.
- Surgical repair of physically injured parts of the body

Pharmacologic

- Treatment of infection such as gonococcal, trichomonas and chlamydial **Ceftriaxone**, 250 mg IM in single dose

  PLUS

- **Metronidazole**, 2gm orally in single dose,

  PLUS

- **Doxycycline**, 100mg P.O., BID for 7 days

In Child Abuse

- **Ceftriaxone**, 125-250mg IM

  OR

- **Erythromycin**, 250mg P.O., TID seven days

Prevention of Pregnancy: provide emergency contraception, within 72 hours after exposure

- **Levonorgesterol** two 0.75mg tablets to be taken 12 hours apart.
- **Combined oral contraceptive pills with 50-mcg oestrogen,** two tabs 12 hours apart for two doses.
- **Combined oral contraceptive pills with 30-mcg oestrogen,** four tabs 12 hours apart for two doses.

- **IUD** insertion up to 5 days following exposure. Screen for infection and pregnancy before inserting IUD
- **Post Exposure Prophylaxis (PEP) for prevention of HIV infection: *refer guideline***

23.3.9 NEONATAL RESUSCITATION

Most episodes of birth asphyxia can be anticipated based on high risk antepartum and intrapartum factors. For effective resuscitation, it is important to anticipate the need for resuscitation and prepare equipment and personnel.

ANTEPARTUM FACTORS THAT CALL ATTENTION TO PREPARE FOR RESUSCITATION INCLUDE:

- Maternal diabetes
- Pregnancy induced hypertension
- Maternal chronic illness
- Previous Rh-sensitization
- Polyhydramnios or oligohydramnios
- Maternal infection
- Poor obstetric history including difficult or operative delivery, abortion, still births, low birth weight babies, developmental defects etc.
- Multiple gestation and post-term gestation
- Maternal medicine treatment like reserpine, lithium carbonate, diazepam etc.
- Maternal under-nutrition (height < 145cm, weight < 40kg)
- Maternal anemia, Hgb < 8gm%
- Maternal age (<20 years or > 35 years).

The intrapartum factors include:

- Elective or emergency caesarian section
- Abnormal presentation
- Premature labor and precipitous labor
- Rupture of membrane more than 24 hours prior to delivery
- Foul smelling amniotic fluid
- Prolonged labor greater than 24 hours or prolonged 2nd stage of labour greater than 2 hours
- Foetal distress of whatever cause
- Use of general anesthesia
- Narcotics administered to the mother within 4 hours of delivery
- Meconium stained amniotic fluid
- Prolapsed cord
- Antepartum haemorrhage

PREPARATION FOR RESUSCITATION:

For normal term deliveries, a trained person, such as a midwife or nurse, should be capable of at least providing Bag and Mask ventilation. A radiant warmer or simple room heater, preheated mattress, dry clothes should be ready for use. All resuscitation equipment should also be immediately available and in working order. When asphyxia is anticipated, trained health workers capable of intubating the baby (e.g. pediatrician) should attend the delivery. If pediatrician is not available, an obstetrician or a general practitioner who is trained to intubate the newborn baby should attend the delivery. All equipment should be ready for use.

EQUIPMENT AND MEDICINES THAT NEED TO BE READY INCLUDE:

- Radiant warmer, sterile sheets
- Suction catheters

- Suction machine
- Infant resuscitation bag
- Appropriate size face-masks
- Laryngoscope with blade
- Endotracheal tube (2.5, 3.0, 3.5, and 4.0)
- Scissors, adhesive tape, gloves and stethoscope
- Syringes of different sizes
- Needles
- Alcohol and iodine
- Umbilical catheters of 5F to 8F
- Feeding tubes
- IV cannula (24G) and 3-way connectors, if available

Other equipment/medicines may be needed based on the specific condition and situation of the newborn.

Initial steps of neonatal resuscitation

For most normal deliveries, all that is required is Essential Newborn Care (ENC); drying, warming, cord care, eye care and initiation of breast milk within the 1st one hour of life.

Note: In every case of neonatal resuscitation, remember that a delay or ineffective resuscitation can lead to an increased chance of brain damage and make resuscitation more difficult.

PROCEDURES OF INITIAL STEPS OF RESUSCITATION: OPEN AIRWAY:

- Place on back in horizontal position with neck slightly extended (may use shoulder roll). Both hyperextension and under-extension of the neck can compromise air entry.

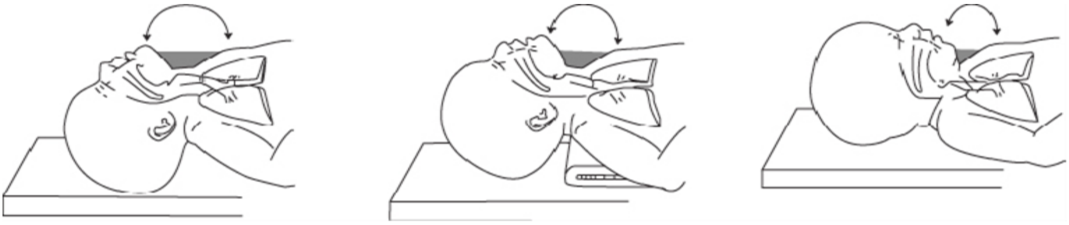


Figure: 22.1. Hyperextended slightly extended flexed

- Suction mouth, then nose
- Start bag and mask ventilation

BAG AND MASK VENTILATION

Indications

- No spontaneous breathing at all
- Gasping respiration
- Recurrent apnea or irregular breathing

CONTRAINDICATION TO BAG AND MASK VENTILATION

- Diaphragmatic hernia
- Baby born with thick meconium stained liquor

Cautions:

- Select the proper size mask, which should cover from the tip of the chin to the nose in an air tight manner.
- Ensure neck is slightly extended and there are no secretions.
- If bag and mask ventilation is given for > 2 minutes, insert and oro-gastric tube
- If HR>100bpm and respiratory efforts are good, stop ventilation and provide free flow oxygen. Continue monitoring HR, respiration and color.
- If HR is 60-100bpm and increasing, continue ventilation.
- If HR is 60-100 and not increasing, continue ventilation and start chest

compression.

- If HR < 60bpm, continue ventilation and start chest compression

ADRENALINE

Indication:

- Heart rate < 80bpm after 30 seconds of chest compression along with positive pressure ventilation with 100% oxygen
- If heart rate is zero

○ Dose: 0.1 – 0.3ml/kg of 1:10,000 solutions

Route: Intravenous or intra-tracheal. Give as rapid as possible. After 30 seconds of giving adrenaline, check the heart rate. If the heart rate is still <100bpm, consider repeating adrenaline.

23.3.10 RECOMMENDED IMMUNIZATION SCHEDULE

Table: 23.3. Recommended schedule for immunization according to EPI program

Age	Vaccination
Birth	BCG OPV-0
6 weeks	OPV-1 , DPT1-HBV1-Hib1 (Pentavalent)
10 weeks	OPV-2, DPT2-HBV2-Hib2 (Pentavalent)
14 weeks	OPV-3, DPT3-HBV3-Hib3 (Pentavalent)
9 months	Measles

Table: 23.4. Recommended schedule of immunization for children attending clinic at later age but before 5 years

Age	Vaccination
First visit	BCG if Mantoux test is negative OPV-1 DPT1-HBV1-Hib1 (Pentavalent)
Second visit (after one month)	OPV2 DPT2-HBV2-Hib2 (Pentavalent)
Third visit (after one month)	OPV-3 DPT3-HBV3-Hib3 (Pentavalent) Measles

Table: 23.5. Hepatitis B vaccine doses

Vaccine	Type of vaccine	Route of administration	Adverse reaction
BCG	Life attenuated	Intradermal	BC Gioma
DPT-HBV-Hib **(Pentavalent)**	Toxoid (DT) Inactivated bacteria (P) Protein conjugated polysaccharide (Hib) Recombinant product (HBV)	IM	Fever, anaphylaxis, crying, & shock
OPV	Life attenuated virus	Oral	Paralysis
Measles	Life attenuated virus	Subcutaneous	Fever

Engrix B 10 microgram is also available and three doses are recommended (at birth, at one month and at six months of age). Booster dose is given after 10 years.

23.3.11 FEEDING PROBLEMS

Feeding of normal baby:

The mother should be instructed to start feeding the baby within one to two hours after delivery. The first feed should be the breast milk and there is no need for any test feed with water or dextrose. The first few feeds should be supervised and records of feeds should be documented.

Feeding of a preterm, small for date (SGA) and infants of diabetic mothers (IDM): Infants less than 1500 grams should receive all the fluids and calories intravenously for the first 24 hours. SGA and IDM babies should be started feeding by one hour of age, First few feeds may be given by NG tube and they should be fed at least two hourly if sucking is poor. Once sucking is well established and blood sugar is normal these babies should be given to the mother for supervised breast feeding.

Feeding of term asphyxiated infants:

Mildly asphyxiated infants should feed like any healthy baby, but must be closely supervised for the first 12 hours. Babies with severe asphyxia should be started with 2/3 maintenance IV fluids and strict intake records should be maintained routinely.

Evidence for adequate nutrition

Weight gain should be 20–30g/kg/day for premature infants and 10g/kg/day for full term infants.

Adequate growth requires:

- 100-120kcal/kg/day in term infants
- 115-130kcal/kg/day for preterm infants
- 150kcal/kg/day for very low birth weight infants

23.3.12 FLUID AND ELECTROLYTE

Normal maintenance requirements (volume of fluid/kg/day)

- Day 1: 60 m1/kg/day
- Day 2: 80 m1/kg/day

- Day 3: 100 m l/kg/day
- Day 4: 120 m l/kg/day
- Day 5: 140 m l/kg/day
- Day 6 & above: 150 m l/kg/day

Additional allowance:

- Increase insensible water loss:
- Radiant warmer: 20 m l /kg /day
- Photo therapy: 20 m l /kg /day
- Increase body temperature: 10-20 m l /kg/day

Increase loss of water from other routes:

Example: neonatal entrocolitis, GI aspirates diarrhoea. The loss in the above conditions are variable, they should be replaced volume for volume.

Stomach contents should be replaced with half saline with KCL loss. Small intestinal contents should be replaced with Normal saline and KCL.

23.3.13 KANGAROO MOTHER CARE

Kangaroo Mother Care (KMC) is defined as early, prolonged and continuous skin to skin contact between a mother and her low birth weight infants (LBWI), both in hospital and after early discharge until at least the 40th week of postnatal gestational age. KMC does not need sophisticated equipment, and for its simplicity it can be applied almost everywhere including peripheral hospitals. Kangaroo Mother Care also contributes to the humanization of neonatal care and the containment of cost, for which reason it may also be attractive for neonatal units in high-income countries.

Kangaroo care a program of skin-to-skin contact between mothers (or any family member) and a LBWI is part of the revolution in the care of premature infants.

The benefits of Kangaroo Mother Care: Many studies showed that Kangaroo Mother Care offers the preterm infants many physical and emotional benefits, which includes:

- A stable heart rate
- More regular breathing
- Improve dispersion of oxygen throughout the body
- Prevention of cold stress and also warming babies who are already in cold stress, Kangaroo transportation where transport incubators are not there to keep the warm chain.
- Longer period of sleep (during which the brain matures).
- More rapid weight gain and earlier discharge from hospital.
- Reduction of purposeless activity which simply burns calories at the expense of infant's growth and health.
- Decreased crying.
- Opportunities to breast feed and enjoy all the healthful benefits of breast milk.
- Earlier bonding

The KMC works so beautifully because of three factors affecting the infant:

- It creates conditions similar to those with which the infant had become familiar in utero, such as the proximity of the mother's heart beat sounds and her voice coupled with the gentle rhythmic rocking of her breathing
- It provides containment and allows for flexion and prevents heat loss and provides heat from skin to skin contact.
- Protects the infant and offers a reprieve from the stressful elements of NICU.

WHEN TO DISCHARGE FROM KANGAROO POSITION:

The decision of discharging from Kangaroo position is made by the baby itself (at about the 40th week (gestational age + postnatal age) and weight of about 2000 grams. When the baby is restless and the mother can no longer maintain the Kangaroo position, it is time to take the baby out of the kangaroo "pouch".

Further reading

Management protocol for selected Obstetrics conditions, FMOH, 2014

Standardized Treatment Guideline for Ethiopia, FMOH, 2014

CHAPTER 23:

PALLIATIVE CARE

- Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

PALLIATIVE CARE:

- Provides relief from pain and other distressing symptoms;
- Affirms life and regards dying as a normal process;
- Intends neither to hasten nor postpone death;
- Integrates the psychological and spiritual aspects of patient care;
- Offers a support system to help patients live as actively as possible until death;
- Offers a support system to help the family cope during the patient's illness and in their own bereavement;
- Uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated;
- Will enhance quality of life, and may also positively influence the course of illness;
- Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

23.1 PAIN MANAGEMENT

SECTION A: CAUSES OF PAIN, ASSESSMENT AND TREATMENT

The International Association for Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

The concept of total pain refers to the global nature of pain perception not only as a physical ailment but that it has a psychological, spiritual and social consequences.

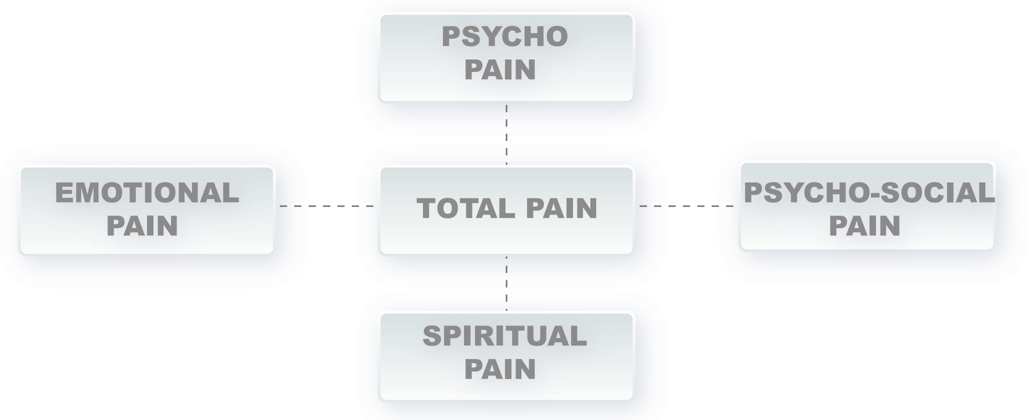


Figure: 23.1.The concept of Total Pain (first described by Cecily Saunders)

CAUSE AND CLASSIFICATIONS OF PAIN

- **Acute versus chronic pain**
    - **Acute pain** is due to a definable acute disease or injury, duration limited to healing of tissue in days or weeks, accompanied by anxiety and sympathetic over-activity (sweating, tachycardia, tachypnea).
    - **Chronic pain** on the other hand persists months beyond the usual course of an acute disease reasonable time for an injury to heal, or is associated with a chronic pathological process which causes continuous pain or pain which recurs at intervals for months or years. It is accompanied by psychological problems such as depression but no

sympathetic response due to adaptation of the sympathetic nervous system.

- **Neuropathic versus Nociceptive Pain**
    - **Neuropathic pain** is caused by damage to the central or peripheral nervous system. Neuropathic pain can be caused by injury, compression or infiltration of a nerve. Often neuropathic pain is described as a burning, tingling or stinging sensation or a shooting electric shock-like sensation – 'pins and needles'.
    - **Nociceptive pain** arises from noxious stimuli, potential or actual injury of somatic or visceral tissues of the body.

ASSESSMENT OF PAIN

Pain should be considered as the **5th vital sign**. A proper assessment of pain is essential for successful treatment. The initial assessment involves the following: detailed history taking including psychosocial assessment, physical assessment, and diagnostic evaluation.

In palliative care there are many different possible causes of pain. It is important to establish the cause of pain. Therapy should be directed at the cause wherever possible. The best approach to differentiate cause and origin is to attempt to characterize pain through the well-known pneumonic **"P Q R S T".**

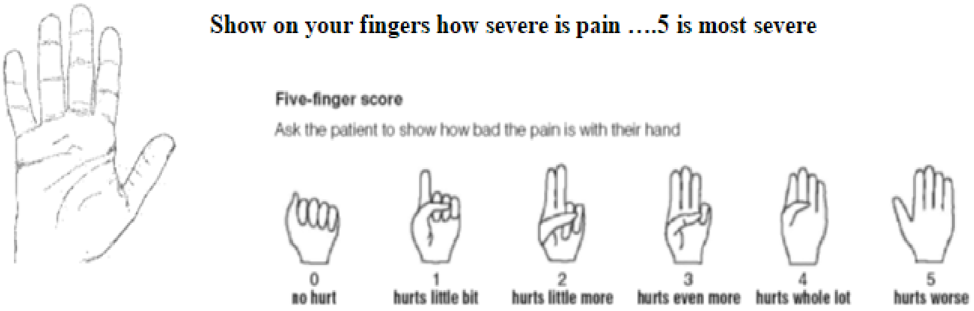
- **P** refers to Precipitating and palliating (relieving) factors
- **Q** refers to Quality of pain (e.g. burning, stabbing, throbbing, aching, stinging)
- **R** to Radiation of pain
- **S** to Site (document on body diagram) and
- **T** to Timing (duration of pain, recurrence, whether constant or intermittent) and Treatment (the effect of current and previous medications)

In palliative care it is not only sufficient to characterize the pain but also measure the degree of severity as objectively as possible. To assess success of treatment some form of quantitation of pain is necessary.

The simplest and most reliable index of pain is the patient's verbal report. For regular follow-up, it will be useful to grade the pain at every visit on a pain scale. Many pain-scoring systems (pain scales) are available, but the numerical scale of ten is the most recommended in adults while the facial scale is effective in pediatric age.

Scales

- *Categorical or verbal rating scale*: A four or five point scale could grade the pain as none, mild, moderate, severe and excruciating etc. This scale is simple to apply but is not sensitive enough.
- *Numerical Scale*: It has 0 at one end meaning no pain and 10 at the other end meaning worst imaginable pain. (No pain) **0** 1 2 3 4 5 6 7 8 9 **10** (Worst possible pain)
- *Visual Analogue Scale (VAS)*: - A100 mm scale with no pain at one end worst imaginable pain at the other is particularly used in clinical trials, as it is more amenable to statistical analysis than numerical scale. It is a simple line on which the patient marks **X** to denote how strong their pain is No pain Worst possible pain
- Palms Pain Scale or Five-finger score (0-5)



Show on your fingers how severe is pain ….5 is most severe

The hand scale

Figure: 23.2. Five-finger score

The hand scale ranges from a clenched hand (which represents 'No hurt') to five extended digits (which represents 'Hurts worst'), with each extended digit indicating increasing levels of pain.

Note: it is important to explain this to the patient as a closed fist could be interpreted as worst possible pain in some cultures.

- For children: *The Faces pain scale*

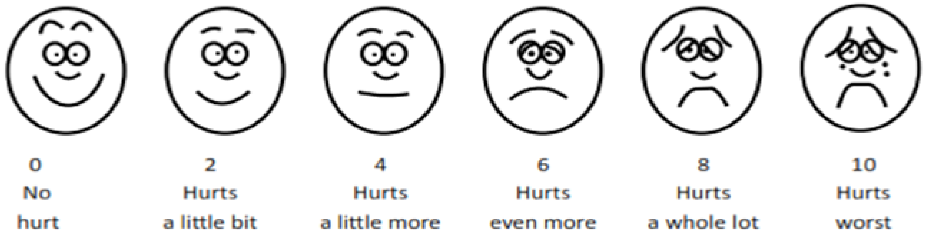


Figure: 23.3. The Faces pain scale for children

(The Faces pain scale has been revised so that the scale is from zero to ten).

- ○ Use with children who can talk (usually 3 years and older)
- ○ Explain to the child that each face is for a person who feels happy because he has no pain, or a little sad because he has a little pain, or very sad because he has a lot of pain.
- ○ Ask the child to pick one face that best describes his or her current pain intensity.
- ○ Record the number of the pain level that the child reports to make treatment decisions, follow-up, and compare between examinations.
- ○ For use in children less than three years of age or older non-verbal children Face pain scale is used to assess pain.

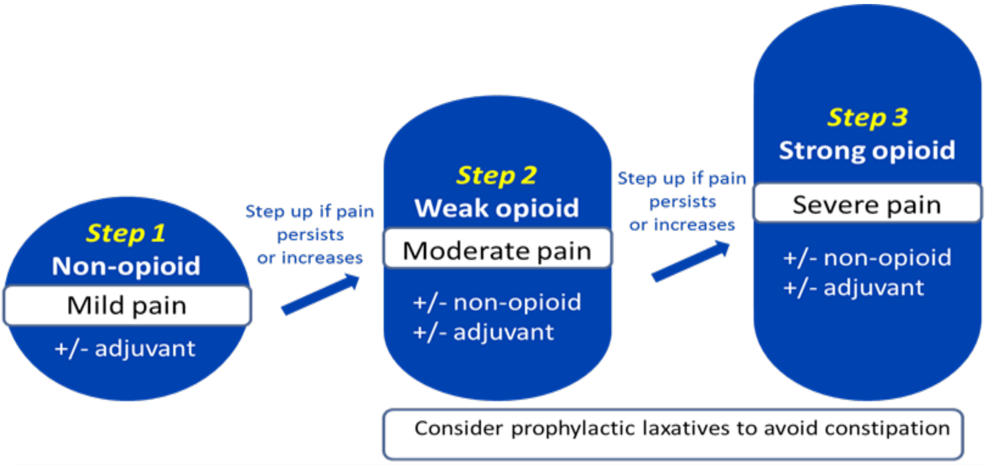
PRINCIPLES OF CHRONIC PAIN MANAGEMENT

- The management of chronic pain involves the use of oral drug therapy by the clock depending on the duration of action of the drug.
- Pain should be treated whenever possible, consider pharmacologic precautions for all analgesic drugs.
- **'By the mouth':** The oral route is best for the management of chronic pain. Oral medications should only be abandoned if the patient is unable to take or retain them.
- **'By the clock':** Analgesics should be given *'by the clock'*, i.e. at regular intervals. Analgesics are given according to a strict schedule determined

by the duration of action, in order to prevent recurrence of pain. A patient on a regular schedule of analgesia will also need to have available a 'breakthrough' dose for any episodes of breakthrough pain.

- **'By the ladder':** the two/three step analgesic ladder (two step for pediatric, three step for adults) which is meant for mild, moderate and severe pain is to be followed. Unless the patient is in severe pain, begin by prescribing a non-opioid drug and adjust the dose, if necessary, to the maximum recommended dose.
- **'For the individual':** the right dose of an analgesic is the dose that relieves the pain.
- **'Attention to detail':** it is essential to monitor the patient's response to the treatment to ensure that the patient obtains maximum benefit with as few adverse effects as possible
- **'Combination therapy'** using two or more analgesia of different mechanism of action is evidence-based practice.

WHO ANALGESIC LADDER


Step 1
Non-opioid
Mild pain
+/- adjuvant
Step up if pain persists or increases
Step 2
Weak opioid
Moderate pain
+/- non-opioid
+/- adjuvant
Step up if pain persists or increases
Step 3
Strong opioid
Severe pain
+/- non-opioid
+/- adjuvant
Consider prophylactic laxatives to avoid constipation

Non-opioids	ibuprofen or other NSAID, paracetamol (acetaminophen), or aspirin
Weak opioids	Tramadol, or low-dose morphine
Strong opioids	Morphine and fentanyl
Adjuvants	antidepressant, anticonvulsant, antispasmodic, muscle relaxant, bisphosphonate, or corticosteroid

Combining an opioid and non-opioid is effective, but do not combine drugs of the same class.

Time doses based on drug half-life ("dose by the clock"); do not wait for pain to recur

Figure: 23.4. The World Health Organization 3-Step Analgesic Ladder for Adults

STEP I: NON OPIOID ANALGESIA

NSAIDs: They have a key role in the management of pain associated with inflammation as in soft tissue infiltration and bone metastases. NSAIDs differ in their effect on platelet function.Aspirin causes irreversible platelet inhibition whereas Ibuprofen, etc. causes reversible platelet inhibition. Diclofenac etc. do not have any commendable effect on platelet function.

The dosage schedule for commonly used NSAIDs is:

- **Diclofenac**: 50mg PO TID
- **Ibuprofen:** 400-600mg TID
- **Paracetamol**: 1 gm Po QID

STEP II: WEAK OPIOIDS

Tramadol: 50-100mg q8h-q6h. Maximum dose is 400mg.

Weak opioids are not recommended for pediatrics age group (see 2 step analgesic ladder)

Low-dose morphine can also be used at Step 2.

STEP III- STRONG OPIOIDS

The dose must be titrated for each individual patient starting from the lowest possible dose in elderly and cachectic patients of 2.5mg/4hourly to normal adults of 5mg/4hourly. There is no standard dose for morphine for the treatment of chronic or cancer related pain and hence no ceiling effect, meaning dose is escalated 72 hours and progressively until pain is controlled and side effects such as nausea and drowsiness are tolerated.Always prescribe a laxative along with an opioid regularly as tolerance is never developed for this particular, and, in selected patients an anti-emetic on as required basis is prescribed if the risk of nausea and vomiting is very disturbing.

Normal release morphine (NR) is always started on four hourly basis and begins to work after about 20 minutes and analgesia lasts four hours. In an opioid naïve patient, start with 2.5-5 mg morphine. Experienced Patients, who are receiving an opioid, may require higher doses (based on equianalgesic doses). It should be given four hourly. A double dose is given at bedtime and the midnight dose is skipped. A rescue dose is advised for breakthrough pain. This should be the same as the four hourly dose of morphine. If these breakthrough episodes persist and become more than 4 /day, dose adjustment as above is required. The dose is increased by 30-50% every 3 days and it can also be reduced progressively in the same manner.

Adverse effects: Even with the therapeutic dose of opioids the following adverse effects are common.

- Constipation occurs in about 95% of patients and it may last as long as the drug is continued. Constipation should be prevented rather than treated and co- administration of a laxative is a must. Bisacodyl 5mg at night, increasing to 15mg if needed) unless the patient has diarrhea.
- Nausea and vomiting occurs in 1/3rd of patients. It is usually seen in the first few days of therapy and is usually self-limiting. Treat with Metoclopramide 10mg tid or Haloperidol 1.5mg once a day.
- Itching is also seen in less than 7% of the patients sometimes respond to 2-3 days of antihistamine therapy, use Chlorpheniramine.
- Other side effects include dry mouth, urinary hesitancy, and sleepiness.

Signs of toxicity: These appear when the administered dose of morphine is more than what is required for pain relief, or when the pain is not morphine-responsive, yet dose is escalated progressively. The signs are toxicity are delirium, myoclonus and drowsiness. Drowsiness occurs in up to 1/3rd of patients on initiation of treatment or following a significant dose increase. If it persists dose reduction is needed. Dose reduction is recommended in renal impairment and old age and debility. These toxicities can be effectively managed with specific drugs including naloxone, an opioid antagonist.

As long as the dose escalation for morphine is made in a stepwise manner, there is less likelihood of an excessive dose being given toxicities are unlikely to occur. But in situations such as renal failure there may be accumulations resulting in toxicities. There are reports where compulsive drug seeking behaviors exhibited by few patients who have a past history of psychiatric illness. With the same token respiratory depression and addiction are NOT also problem with oral morphine in patient with a clear indication. On the other hand, physical dependence is a normal physiological response to opioid therapy, which causes withdrawal symptoms, if the drug is abruptly stopped or an opioid antagonist is administered. Withdrawal symptoms can be effectively managed by gradual and supervised reduction of the opioid therapy.

Naloxone – reverses all opioid side effects, so both respiratory depression and pain relief are reversed. Too much naloxone given too quickly and reversing analgesia may result in restlessness hypertension and arrhythmias and has been known to precipitate cardiac arrest in a sensitive patient.

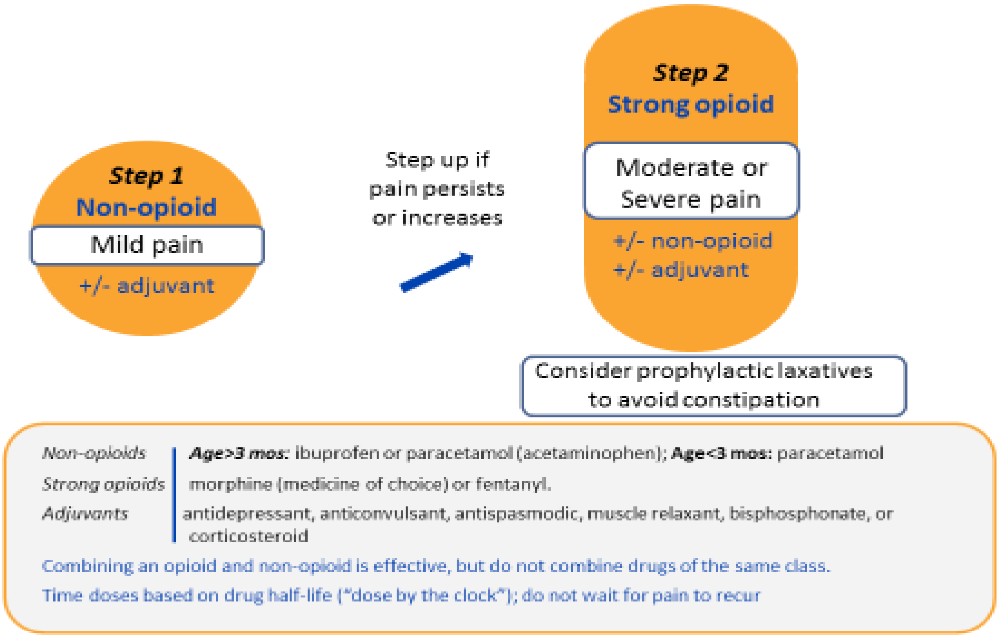
- Indications for Naloxone
    - RR < 8/minute.
    - RR <12/minute, difficult to rouse, cyanosis
    - RR < 12/minute, difficult to rouse, SaO2 <90%

Dose: dilute naloxone 400 micrograms to 10ml with 0.9% saline. Give 0.5ml (20 micrograms) IV every 2min until respiratory status is satisfactory. Further boluses may be necessary because naloxone is shorter-acting than morphine.

Note: There can be concerns when prescribing morphine that addiction can occur. When used correctly, patients do not become dependent, tolerance is uncommon and respiratory depression does not usually occur. The risk of addiction is commonly overestimated by patients and family, so it is important for healthcare workers to alleviate their fears. When discontinuing morphine, avoid symptoms of withdrawal by titrating the opioid dose down slowly.

WHO ANALGESIC LADDER FOR CHILDREN

The two-step approach is an effective strategy for the pharmacological management of persisting pain in children rather than the three-step analgesic ladder used for adults. The two-step approach considers the use of low doses of strong opioid analgesics for the treatment of moderate pain as the benefits of using an effective strong opioid analgesic outweigh the benefits of intermediate potency opioids in the pediatric population and although recognized, the risks associated with strong opioids are acceptable when compared with the uncertainty associated with the response to codeine and tramadol in children.


Step 1
Non-opioid
Mild pain
+/- adjuvant
Step up if
pain persists
or increases
Step 2
Strong opioid
Moderate or
Severe pain
+/- non-opioid
+/- adjuvant
Consider prophylactic laxatives
to avoid constipation

Non-opioids	**Age>3 mos:** ibuprofen or paracetamol (acetaminophen); **Age<3 mos:** paracetamol
Strong opioids	morphine (medicine of choice) or fentanyl.
Adjuvants	antidepressant, anticonvulsant, antispasmodic, muscle relaxant, bisphosphonate, or corticosteroid

Combining an opioid and non-opioid is effective, but do not combine drugs of the same class.

Time doses based on drug half-life ("dose by the clock"); do not wait for pain to recur

Figure: 23.5. The World Health Organization 2-Step Analgesic Ladder for Children

VARIATION FROM THE WHO PAIN MANAGEMENT PROTOCOL

- By mouth administration may not be feasible in dysphagia (sub-lingual or per-rectal or parenteral administration).
- By the clock administration may not be possible as well in cases with renal failure and dyspnea where the dose and frequency should be reduced or spaced. In renal failure, morphine interval may need to be longer or the dose reduced. If no urine output, then morphine should be stopped and given PRN.
- For breakthrough pain – the drug has to be given in between the specified intervals.
- In neonates – half life and clearance are variable.
- A double dose is used at bed time to avoid waking the patient for medication
- By the ladder administration may be difficult in the following instances:

- As in morphine trial for quick pain relief and for assessing the dose requirement.
- Sticking to step 2 weak opioids when morphine is not available.
- Morphine may be used in smaller doses if step 2 are not available.
- Non opioid may be omitted for poor side effect profile.
- Adjuvants may be omitted to minimize the number of drugs.
- Go beyond step 3 in pain that is not responsive

ADJUVANTS FOR PAIN

The adjuvants are not analgesics in the true pharmacological sense, but may contribute significantly to pain relief whether used alone or in combination with the analgesics on the WHO 2/3-step ladder and they may have an analgesic sparing effect. Adjuvant analgesics are of particular use in pain that is partially opioid-sensitive pain. Pain that is less sensitive to opioids includes neuropathic pain, bone pain, pain associated with inflammation and sepsis. Pain associated with smooth or skeletal muscle spasm will not respond to an opioid and will need an adjuvant analgesic. Pain related to anxiety will also benefit from adjuvant analgesics.

- ***Anti-Depressants and Anti-Convulsants:*** Helpful for neuropathic pain, which may present as burning, pricking, allodynia, paresthesia or sharp, shooting pain.

Amitriptyline: 25mg PO at night. Increase dose as needed.

OR

Carbamazepine: 200 mg PO at night. Increase dose as needed

OR

Gabapentin: 300 mg PO at night. Increase dose as needed.

- ***Corticosteroids:*** are used as adjuvant treatment if neuropathic pain is suspected to be due to nerve compression e.g. by tumor or inflammation

Dexamethasone: 4 mg daily

OR

Prednisone: 40-60mg daily

- ***Muscle relaxants/Anxiolytics:*** are used as an adjuvant for skeletal muscle spasm and anxiety- related pain.

Diazepam: 5mg orally, 2-3 times per day.

- ***Antispasmodics:*** are helpful in relieving visceral distension pain and colic.

Hyoscine Butylbromide: 10mg three times /day PO or IM; can be increased to 40mg three times/day

Non-Pharmacological management of pain

Palliative care includes many non-pharmacological ways to manage 'total' pain. These therapies address the physical, psychological, social and spiritual dimensions of pain.

The following are a few holistic non pharmacological ways of treating pain.

- Anything that enhances quality of life can, in turn, relieve pain.
- Listening and empathy.
- Counseling – provides emotional support and practical suggestions.
- Companionship and accompaniment – can help ease pain and increase comfort.
- Activities such as favorite music, games, gardening, memory book – provides meaning and distraction.
- Spiritual/pastoral support and prayer – provides comfort, meaning and hope.
- Positioning – enhances comfort and relieves pressure areas.
- Bathing, grooming, and other care measures – enhances comfort and self-respect.
- Exercise – improves mobility, circulation and skin integrity.
- Massage, therapeutic touch.
- Traditional therapies that are beneficial, healing and comforting.

- Heat/cool applied locally – can reduce swelling and help relaxation.
- Treatments such as radiotherapy can reduce inflammation, pain and tumor size

PHYSICAL CARE II - SYMPTOM MANAGEMENT

Symptoms of various illnesses have for a long time been considered 'sign posts', and merely indicators to a disease and not important by themselves. This common practice is illustrated in acute illnesses whereby symptoms vanish with addressing of the underlying illness, for instance, fever and headache in malaria. However, in chronic non-curable diseases, symptoms may persist long after the diagnosis of disease, as a result of chronic complications, and, are not always useful indicators of underlying conditions and only contribute to suffering and poor quality of life to those affected. Hence it is strongly advised to control them. The general approach to symptom control in palliative care includes assessment and investigation for the undiagnosed disease and severity of the symptom, treatment of reversible causes, initiation of disease/ symptom-specific medicines and non-drug measures as well as involvement of the patient and family in the management plan.

The common symptoms in palliative care are:

- Fever
- Respiratory Symptoms
- Gastrointestinal Symptoms
- Urinary Symptoms
- Skin and Wound Care

23.2 FEVER

Fever is elevation of core temperature above 37.4 degree Celsius as measured at the axilla.

Table: 23.1. Common cause of fever and its management

Common Causes	Management
• Infections • Inflammatory (autoimmune) • Metabolic • Malignancy • Drugs & toxins	• If new fever, consider cause, work up and treat properly • If bacterial infection treat with appropriate antibiotics • If malaria treat with antimalarial • If neoplastic in origin, treat with appropriate chemotherapy • If transfusion related, discontinue and treat and work up • **For adults**: Give paracetamol 1 gm every 6 hours (no more than 8 tablets of paracetamol in 24 hours). • **For children**: Provide paracetamol 10-15mg/kg oral per dose, maximum 6 dose in 24 hours. • **Neonate** 5-10mg/kg per dose max of 4 doses in 24 hours, avoid aspirin. • Alternative to reduce fever are NSAIDs (Ibuprofen, avoid if less than 3 months). • Make sure patient stays hydrated. **Home Care Advice** • The sick person will lose a lot of water through sweating; therefore encourage him or her to frequently • Drink water, diluted tea, fruit juices and make sure patient stays hydrated. • To cool the body temperature, wipe the body with lukewarm water (cloth soaked or give a bath). • Encourage febrile patient to wear only light clothes. • Paracetamol can be used as above • *Advice: Seek help if fever does not improve or recurs after treatment. Also if fever is accompanied by cough, diarrhea, severe pain, confusion, night sweats, rigors, stiff neck or unconsciousness.*

RESPIRATORY SYMPTOMS

Dyspnea or breathlessness is a subjective sensation that patients describe as chest tightness, breathlessness, air hunger, inability to take a deep breath, a feeling of suffocation or smothering, or an inability to get enough air. The symptoms usually worsen with exertion and often limit the patient's activity.

Table: 23.2. Approach to Reversible causes of dyspnea /shortness of breath

Possible causes of Dyspnea	**Classical signs and symptoms**	**Treatment**
Bronchospasm/ asthma	Shortness of Breath Non-productive cough Wheezing Decreased air entry	Bronchodilators: Salbutamol Corticosteroids Oxygen therapy
COPD (emphysema/ chronic Bronchitis)	Shortness of Breath Productive Cough Wheezing Decreased air entry	Bronchodilators: Salbutamol Corticosteroids Oxygen therapy Pulmonary rehabilitation Morphine
Congestive Heart Failure	Orthopnea, Proximal Nocturnal Dyspnea, Fatigue, Chest pain, Edema, Inspiratory rales, Elevated Jugular Venous Pressure	Diuretics Cardiac medications *If indicated*, oxygen

Cardiogenic Pulmonary Edema	Severe SOB, Orthopnea, PND, fatigue , Inspiratory rales, Edema, Elevated JVP	Oxygen Diuresis Morphine Treatment of Underlying cause
Bacterial Pneumonia	Cough Fever, chills pleuritic chest pain Localized rales or signs of consolidation	Antibiotics Cautious hydration *If indicated*, oxygen
Tuberculosis	Fever, cough, sweating, chest pain, Weight loss, loss of appetite.	Anti TB, *if indicated Corticosteroid* and oxygen
Pleural Effusion	SOB, chest pain Dullness and decreased air entry with radiographic or ultrasound confirmation	Thoracentesis If indicated chest tube insertion Pleurodesis if indicated Management of underlying disease
Upper Airway Compression	Severe shortness of breath Stridor – especially inspiratory Risk factors, such as neck or mediastinal mass	Corticosteroids Small dose Benzodiazepines, Opioids, or Barbiturates for anxiety or sedation *If indicated, consider/refer:* External radiation Tracheostomy/Airway stent

Copious airway secretions/ Bronchiectasis	Coarse crepitation, Ineffective or absent cough	Anticholinergic drugs Antihistamines If indicated antibiotics Rehydration Airway Suctioning
Pulmonary Embolism	Sudden onset of shortness of breath Chest pain Risk factors for venous thromboembolism e.g. like bedridden patients	Anticoagulation: Heparin *with* Warfarin Oxygen Morphine
Lung Interstitial Pneumonia	Shortness of breathing, hepatosplenomegaly, parotid enlargement, cyanosis and clubbing	Oxygen If indicated Corticosteroid Bronchodilators

Note:

- Give small dose oral morphine—this can reduce dyspnea in end-of-life care. Monitor closely but do not let fears of respiratory depression prevent trying this drug.
    - For a patient not on morphine for pain give 2.5 mg.
    - For a patient already on morphine increase the dose by 25%. If this does not work, increase by another 25% till the patient condition improves (read reference on dose limit for dyspnea).

DYSPNEA HOME CARE

In addition to the treatment given by health worker:

- Help the sick person sit in the best position
- Use extra pillows or some back support
- Open windows to allow in fresh air
- Fan with a newspaper or clean cloth
- Give patient water frequently (it loosens sputum)
- Avoid crowding, cooking and smoking in the room of the patient

MANAGEMENT OF PULMONARY SECRETIONS

Pulmonary secretions associated with pulmonary infections or chronic bronchitis can produce troubling symptoms for patients, particularly as their increasing weakness and fatigue make coughing exhausting and ineffective. For patients who are still able to cough effectively, interventions should be directed at helping to reduce the exertion required to bring up secretions or reducing excess secretion.

- Use an anti-secretory drug to reduce production of respiratory secretions: Hyoscine butylbromide 20 mg stat and 20–40 mg PO TID.
- Humidified oxygen. Inhaled oxygen is a helpful comfort measure to reduce symptoms of upper airway drying when oxygen is being administered.
- Postural drainage: Chest physiotherapy appropriate to the patient's condition is valuable in managing respiratory secretions. Teach caregivers this technique and encourage them to make a special effort to avoid flat or supine positions that allow pooling of secretions in the pharynx or larynx, and to reposition the patient frequently.
- Hydration: Dehydration can increase sputum viscosity and exacerbate difficulties with expectoration. Hydration—orally or intravenously is useful treatment to this problem.

Cough

Table: 23.3: Common cause of cough and its management

Common Causes	Management
Respiratory infections • Bronchospasm • Bronchial obstruction • Cardiac causes • Drug related like ACE inhibitors • Esophageal reflux • Foreign body aspiration	**Treatment of underlying cause** • Treat infections using appropriate anti-infective agents, evaluate for tuberculosis. • Cough from bronchospasm - often responds to bronchodilators including salbutamol with either inhaled or systemic corticosteroids (if indicated) • In patients who are moving little air with each breath, systemic corticosteroids and frequent nebulization of bronchodilators may help. If symptoms improve and tidal volumes increase, hand-held metered dose inhalers may be effective • Steroids, radiation, Surgery chemotherapy • Diuretics, salt and fluid restriction • Avoid ACE inhibitors • H2 receptor antagonists or proton pump inhibitors may be appropriate (for esophageal reflux). **Symptom management** • Use Dextromethorphan syrup (when indicated) • Give Oral morphine (2.5-5 mg) (when indicated) **Home care (Soothing remedies)** • Spice drinks help to relieve some of the many unpleasant symptoms experienced by patients. • Example: • Cinnamon, ginger, and honey are used to soothe the throat and relieve coughing. • Cinnamon: Add one-quarter teaspoon of cinnamon powder to a cup of clean boiled water (about 150–200 mL). • Add sugar or honey to taste. The drink is ready for use. • Ginger: Add one teaspoon of crushed ginger roots or powder to a cup of clean boiling water. Cover and leave for 5–10 minutes. Add sugar or honey to taste and the drink is ready. Drink as desired. • Honey, ginger, and cinnamon: Add one teaspoon of ginger powder or cinnamon powder to 150 mL honey and stir. • Take 5–10 mL of the mixture 4-hourly for 5 days.

GASTROINTESTINAL SYMPTOMS

Hiccups

Persistent hiccups are not unusual in terminally ill patients and can be a distracting and distressing symptom. The interruption of normal activity in patients with intractable hiccups can cause depression, sleep deprivation, decreased oral intake, and weight loss.

Table: 23.4: Common cause of Hiccups and its management

Common Causes	Management
• phrenic nerve or diaphragmatic irritation by tumor • Gastric distension • Gastro-esophageal reflux, • Severe esophageal candidiasis. • Drugs (benzodiazepines, corticosteroids, barbiturates) • Psychogenic • intracranial mass/lesion	**Treat the underline cause** **Symptomatic management (pediatric dosage)** • Metoclopramide (10 mg tablet, 1-2 tablets three or four times daily 7-10) /dose • For children-0.1-0.2mg/kg/dose 4 times daily • Chlorpromazine 25mg PO tid up to 7-10 days (for children 0.5-1mg/kg) • Haloperidol (5 mg tablet: 1/4 to ½ tablet once to three times daily). • If patient has brain tumor, try antiepileptic medication (like phenytoin). • Drinking cold water, cold water gargling, Valsalva maneuver **Home care** Stimulate the throat: • Quickly eat 2 heaped teaspoons sugar, or • Drink cold water or eat crushed ice, or • Rub with a clean cloth inside the top of the mouth (feel toward the back, where the where the top of the mouth is soft). Interrupt the normal breathing: • Hold breath or breathe into paper bag, stop when you feel uncomfortable. • Pull knees to chest and lean forward (compress the chest).

NAUSEA AND VOMITING

Conduct a detailed history of the patient's illness including duration of symptoms, precipitating events, what has been tried to alleviate symptoms, and what has been most useful in management of these symptoms.

- Evaluate current medications noting those with known GI side effects.
- Assess for possible infectious conditions
- In women in child bearing age, consider pregnancy
- Increased intracranial pressure can present with nausea and vomiting
- Perform a thorough physical exam to localize the symptoms
- Look for surgical causes of nausea and vomiting
- Presence of fever and signs of dehydration (e.g., hypotension) indicate a more serious process.

Table: 23.5: Management of nausea and vomiting

i. Treatment for reversible causes	
Nausea and vomiting secondary to Infection or Drug side effects	- Treat infections with appropriate antimicrobials and Address drug side effects
ii. Symptomatic management of nausea and vomiting	
1. Antiemetic	
Dopamine Antagonists	- Most commonly used as first line. - The prototype agents for this class are 1. Metoclopramide: 10 mg every 8 hours For children use 0.1-0.2mg/kg/dose 4 times daily 2. Haloperidol & Chlorpromazine which exerts its effects centrally (1-2 mg once daily and 25-50mg every 6-12 hours respectively

Histamine Antagonists	- Promethazine 25mg 1-4 times daily (For children 0.5mg/kg/dose)
Corticosteroids (for intractable vomiting)	- Add Dexamethasone 10mg/m^2 /dose once daily.
Serotonin antagonist (for intractable vomiting)	- Ondansetron 8mg tid
2. Rest Gut	IV fluids -Sometimes it is best to 'rest the gut' by administering intravenous fluids that may contain replacement electrolytes and basal metabolic energy (e.g.40% dextrose) as needed Keeping NPO
3.Reduction of Increased Intracranial Pressure (ICP)	ICP is often an emergency. Treat the Cause - Nursing care-head elevation 30^0 above horizontal - Give dexamethasone 4-8mg q8 hours to decrease the pressure as indicated, give Mannitol IV 1-1.5g per kg. - For Cryptococci do lumbar puncture as required
III. Home care	
	• Give clear liquids initially and boil water if not filtered; advance to full liquids as tolerated. • Give small, frequent meals. • Encourage breast feeding in infants and young children • Let the patient select the type of food he prefers Avoid fried and fatty foods. • Keep patients away from the place where food is being cooked (to avoid smell and sight of food). • Encourage patient to be in a sitting position after eating for at least 30minutes. • Seek help from trained health worker for • Vomiting more than once a day, or dry tongue, or passing little passing little urine or abdominal pain.

DRY MOUTH (XEROSTOMIA)

Dry mouth (Xerostomia) is a condition whereby salivary flow is reduced due to reduced productionor free flow. This aggravates a dry mouth resulting soreness and difficulty of speech and mastication.

Table: 23.6: Common causes of Dry Mouth (Xerostomia) and its management

Common Causes	Management
• Dehydration, • Mouth breathing • Reduced mastication • HIV-related (OI) infections • anxiety, and depression • Oxygen therapy • Salivary gland diseases • Drugs(antihistamines, anticonvulsants, antidepressants, and anticholinergic) • Radiotherapy which reduce salivary flow	**Treat the underline cause** • Treating reversible causes • Treat infections and review drug regimens • Idiopathic or aphthous ulcers can be treated either with a course of Corticosteroids. **Symptomatic management at Home** • Check the mouth, cheeks, palate, gums, tongue, and teeth often to identify and manage any problems early. • Seek help from health worker if dry mouth persists • Take regular sips of water to keep up fluid intake • Keep lips clean, soft, lubricated, and intact as far possible. • Apply petroleum jelly or moisturizing lotion to lips • Brush teeth with a chew stick or a small, soft • Toothbrush (a baby's toothbrush is ideal) after each meal and at night. If available, use fluoride toothpaste. • If brushing is not possible due to pain or bleeding, use soft sponges, cotton buds, or a gloved • finger wrapped with gauze or a soft cloth • Use a mouthwash after each meal and at night (in addition to brushing, not as a substitute). • Avoid a mouth wash that contains alcohol as it dries out the mouth. • Rinse with 15 mL for 60 seconds using alcohol free mouth wash solutions. Suggestions for mouthwash: Saline: 1 teaspoon salt in 500 mL boiled, cooled water Vinegar or lemon juice: 1 teaspoon in one liter of boiled, cooled water. Antimicrobial mouthwashes: 0.2% chlorhexidine gluconate mouthwash Sodium bicarbonate mouthwash if available: 1 teaspoon in 500 mL boiled, cooled water

NUTRITION AND WEIGHT LOSS

General Principles

Nutrition support has been shown to benefit palliative care patients by reducing physical deterioration, improving quality of life, and preventing the emotional effect of "starving the patient to death."

- Palliative care patients of all age groups should be educated and encouraged to consume the following food groups (carbohydrates, proteins, vitamins, minerals, fats & oils, dietary fiber and water).
- The successful management of these medicine-food interactions requires understanding clients' individual food access as well as eating habits. Locally available foods are recommended.
- Management of patients shall include assessment and counseling on feeding with regard to the nutritional needs specific to the stage of the illness.
- Patient and carers shall be counseled on appropriate feeding according to the stage of the illness
- Weight loss is an extremely common symptom in chronic illness.

Table: 23.7: Possible Causes of Weight Loss and Malnutrition in chronic illnesses

Mechanisms	Possible causes
Decreased intake of nutrients	• Insufficient resources to procure food (Poverty) • Dysphagia or odynophagia • Anorexia, nausea, or vomiting • Emotional factors (depression, loneliness or grief) • Dementia
Excessive nutrient loss	• Chronic illness • Malabsorption or drug-related diarrhea

Table: 23.8. Management of Symptoms Causing Weight Loss

Symptom/ setting	Dietary Advice
Loss of appetite	• Drink high-energy drinks (e.g. milk or yoghurt) • Eat small, frequent meals. • Encourage exercise if possible.
Nausea and vomiting	• Eat small, frequent meals. • Restrict intake of fluids after meals. • Eat cold foods or food at room temperature. • Avoid excessively fatty meals. • Avoid lying down after eating. • See relevant section
Sore mouth/ throat	• Eat soft moist foods, (e.g., mashed potato, minced meat). • Use margarine, butter to moisten cooked food (if diarrhea not present). • Avoid sticky foods (e.g., peanut butter). • Avoid dry, rough foods, (e.g. raw vegetables). • Avoid citrus fruits (e.g. lemon, orange, pineapple) and spicy foods. • Eat foods either cold or at room temperature. • See relevant section

Diarrhea	• Eat small, frequent meals. • Drink plenty of isotonic fluids. • Decrease/avoid milk and dairy products. • Fermented dairy products may be tolerated • Decrease high-fat foods • Include foods high in soluble fiber (e.g. bananas, oats). • Avoid caffeine, (e.g. coffee). • Avoid soft drinks (e.g. Mirinda, Coca Cola) • Use anti-diarrheal agent in adults if there is no contraindication • See relevant section
Home Care	• Encourage the sick person to eat, but do not use force as the body may not be able to accept it and he or she may vomit. • Offer smaller meals frequently of what the sick person likes. • Accept that intake will reduce as patient gets sicker and during End-of-life care. • Seek help from trained health worker if you notice rapid weight loss or if the sick person consistently refuses to eat any food or is not able to swallow.

- If all other means fail, try Prednisone 5-15 mg daily in the morning to stimulate appetite in end of life care, stop if no effect after 2 weeks.

DYSPHAGIA AND ODYNOPHAGIA

Difficulty of swallowing food as a result of pain or obstruction due to various causes affects the nutritional status and general health of certain chronic diseases.

Table: 23.9: Common cause of Dysphagia and Odynophagia and its management

Common Causes	Management
• Oropharyngeal problems ○ Candidiasis ○ Mucositis ○ Dry mouth ○ Neurogenic (Stroke, brain tumors or peripheral neuropathies) ○ Pharyngeal abscess, tumor, tonsillitis • Esophageal problems ○ Inflammatory/infection (Reflux esophagitis, candida Herpes, CMV, aphthous ulcer, caustic ingestion, radiation mucositis). ○ Neoplastic (esophageal ca) ○ Motility disorder(e.g. achalasia) ○ Anatomical (hernia, diverticulum stricture) Psychogenic	• Treating reversible causes • Complications like dehydration, electrolyte • disturbance, malnutrition • Symptomatic treatment • Prescribe analgesia • Steroids to reduce inflammation or edema. • If no effect by the third day, stop treatment. • Nasogastric tube,not recommended for long term use due to patient discomfort • Endo-esophageal tube • Gastrostomy tube –contraindicated in Advanced disease Home care • Soft diet to decrease discomfort such as yoghurt or • Depending on what the patient feels is helpful. • Avoid extremely hot or cold or spicy foods. • Upright position to facilitate swallowing Seek help from health worker for persistent sores, smelly mouth, white patches, decreased urine output or difficult of swallowing.

DIARRHEA

Diarrhea is defined as the passage of loose stool three or more times in 24 hours. It can be classified as: **Acute** when the diarrhea lasts for two week or less; **Persistent** when the diarrhea last for two to four weeks or as **Chronic** diarrhea lasting more than four weeks

Table: 23.10: Common cause of diarrhea and its management

Common Causes	Management
- Osmotic - (lactose intolerance and laxative) - Motility(drugs) - Secretory (Cholera)	**I. Treating Reversible Causes**. **II. Prevent dehydration** Correct dehydration by ORS, drink extra fluids and intravenous fluids may be appropriate in a patient with severe dehydration secondary to severe acute or Chronic diarrhea. Decisions should be made on a case-by-case basis. **III. Symptomatic treatment** Symptom treatment is recommended: • If the diarrhea becomes chronic and is not helped by specific treatment • Contraindications for anti-diarrheal agent • It should not be used if there is fever or blood in the stool • Should be avoided in children under the age of one year old. For symptom control, start with anti-motility agents such as: • Loperamide 4mg once, then 2mg per loose stool to maximum 16 mg/day, • Oral morphine 2.5–5 mg every4 hours *(alternative)* **IV. Home care** Advise the patient and caregivers to: Boil drinking water and store it in a clean container with a cover. Wash hands with water and soap before eating food and after visiting a toilet. Give the sick person drinks frequently in small amounts, such as porridge, water (with food), other soups, or oral rehydration solution (ORS) but avoid soft drinks. Avoid fatty foods, concentrated fruit juices, alcohol, and coffee. Use high-fiber foods such as beans, rice, maize meal, green bananas, whole grain bread and potatoes. ○ Eat bananas and tomatoes (for their potassium) ○ Carrot soup helps to replace vitamins and minerals. Carrot soup contains pectin. It soothes the bowels and stimulates the appetite. ○ Eat 5-6 small meals rather than 3 large ones. ○ Protect the peri-anal skin from excoriation by using petroleum jelly or aluminum hydroxide and keep it clean and dry. **Seek help from health worker if:** • Vomiting with fever • Blood in the stool • Diarrhea continues more than 5 days • If patient becomes even weaker • If broken skin around the rectal area

CONSTIPATION

Constipation usually includes a frequency of fewer than three bowel movements a week, but can also include subjective symptoms such as excessive straining, a sensation of lower abdominal fullness, and hard stools.

Table: 23.11: Common cause of constipation and its management

Common Causes	Management
• Low fluid intake • Irregular bowel habit • Low residue and fiber diet • Limited physical activity • In hospital, unfamiliar toilet arrangements (such as the use of bedpans and lack of privacy can also lead to constipation) • Drugs such as opiates • Medical conditions (diabetes, hypothyroidism, hypokalaemia, rectocele, cerebrovascular accidents, and Parkinson's disease) • Mechanical obstruction • (ColonCa, Kaposi)	**I. Treat specific causes** **II. Symptom management** Constipation in persons with chronic diseases is often related to Medications and, thus, preventive measures are the most successful. If non-pharmacological measures are not effective, laxatives are appropriate although hard stool requires a softener and soft stool requires a peristaltic stimulant, a combination of both is better with Fewer side effects. A variety of different laxatives can be used: • Stimulant laxatives, which cause intestinal motility to increase. • (Commonly stimulant laxatives include, Bisacodyl, 5-10 mg po.) • Emollient laxatives, such as mineral oil and liquid paraffin, which are given orally or by enema that act by penetrating and softening the stool. • Hyperosmolar agents like lactulose 15-30 ml PO or PR twice daily. *(If available also use polyethylene glycol, non-absorbable sugars, or sorbitol)* • Suppositories or enemas can be given; especially when oral laxatives alone are insufficient. **III. Home care** • Encourage high fluid intake and regular bowel habit • Treat mild constipation by increasing the patient's dietary fiber intake to a minimum of 20–35 grams daily (fruits, vegetables, porridge, and locally available high-fiber food) • Take a tablespoon of vegetable oil before breakfast. • Encourage patients to be mobile and provide them with Privacy when using toilet facilities. • Take preventive measures when constipating drugs like opioids are prescribed. Offer drinks often. • If impacted, gently put petroleum jelly or soapy solution In to the rectum. If the patient cannot do it, the caregiver can help— always use gloves. • Seek help from a trained worker if pain or no stool is passed in 5 days.

URINARY SYMPTOMS

URINARY INCONTINENCE

- It is the involuntary loss of urine, which may cause hygienic, physical and/or social problems. It is essential to determine the cause and identify those patients where the incontinence is due to an inability to reach the toilet in time.

Table: 23.12. common cause of urinary symptoms and the management

Common Causes	Management
Urge incontinence: sudden, strong desire to void, frequency, loss of moderate to large volume of urine, nocturia and/or enuresis usually present due to urethral inflammation or irritation. **Stress incontinence**: leakage with physical activity (coughing, laughing, lifting etc.), small volume of urine, and intermittent dribbling due to weak pelvic floor. **Overflow incontinence**: strain to void, sense of incomplete emptying, lower abdominal pain/fullness due to urethral obstruction, or bladder under activity (neuropathy). **Functional incontinence**: inability to reach the toilet in time due to physical, psychological or environmental impediment. **Total urethral incontinence**: local incompetence of the urethral sphincter tumor invasion, fistula or surgery. Central loss of sphincter control, confusion/dementia	I. **Correct reversible factors** • Avoid excessive volume of liquid late in the day, caffeinated drinks, alcohol • Treat medical conditions (delirium, infection, • restricted mobility, impaction, diabetes) • Proper use of medication (carbamazepine, diuretics, • lithium, opioids (overflow) • Correct physical/environmental barriers • Odor: identify cause and treat. I. **Consider disease-specific palliative therapy** • Total urethral incontinence: Regular toileting, • a female urethral catheter or a male sheath catheter may be tried. • Urge incontinence: Timed voiding and anti-cholinergic drugs may be helpful. • Stress incontinence: Support prosthesis such as a ring-pessary or urethral inserts may be useful. • Overflow incontinence: Catheterization (Permanent or intermittent), urethral stenting or surgical interventions should be explored. Referral to an urologist is essential in this instance. • Functional incontinence: surgery, psychological support II. **Institute non-pharmacological interventions** • Patient education (fluid restriction in the afternoon and evening, early intake hours before bed time) • Lifestyle modification (e.g. decreased caffeine) Behavioural modification: timed voiding • calcInvasive devices (e.g. catheter, stent French Gauge(FG) 16 is the smallest useful size for adults, catheters are most appropriate and should be changed every 3-6 weeks. • External collection of urine (diapers) • meticulous skin protection with barrier creams such as • zinc and castor oil is mandatory. • Intermittent catheterisation together with an • absorbent pad. III. **Pharmacologic Therapy** Infection: Microbial Culture and Sensitivity and appropriate antibiotic Barrier preparation to protect the skin (Zinc and castor oil/Vaseline) Relieve constipation (see constipation section) Review medication for medicines which may exacerbate the problem. Referral to appropriate service/ more experienced clinician: Urologist or Gynaecologist

HEMATURIA

- **Blood in the urine (Hematuria)** is a frequent presentation in urological disease.
- Ranging from microscopic hematuria, detected by urinalysis, to clearly visible frank hematuria or passage of clots.

Causes	Management
• Tumor o Renal, ureteric, bladder, prostate. o UTI o Calculi o Trauma • Drug-induced o Warfarin and NSAIDS causing bleeding tendency o Cyclophosphamide causing hemorrhagic cystitis, glomerulonephritis	• Correct **reversible factors** o Treat underlying cause: Once the cause of hematuria is established to be self-limited o Reassure patient and family o Complete evacuation of clots (irrigation with water or saline through large bore urethral Catheter o Cystourethroscopy for diagnosis and cautery if patient fit enough. o We can prevent Cyclophosphamide associated hematuria by sticking to rehydration protocols. o If bleeding is due to drugs –discontinue the causative drug and refer o More severe haemorrhage: consider referral o Blood transfusion based on need • **Clot retention:** o Evacuate clots using large bore (22Fr) Foley catheter and irrigate with saline 0.9% continuously until urine clears. o Cystoscopic bladder irrigations may be needed, referral may be required. o Percutaneous insertion of a suprapubic catheter is contraindicated • **Consider disease-specific palliative therapy** o Palliative radiotherapy o Involve the urologist early in managing this problem

Bladder pain

- **Bladder pain**: more constant pain, from a dull ache in UTI to acute disabling pain and may be a sign of obstruction and retention or excruciating, transient pain due to bladder spasm or urinary retention

Causes	Management
• Cystitis • Urinary obstruction (calculi, clot, BPH, PUV) • Urinary retention Bladder spasm (irritation hyper excitability of trigon) • Local cancer • Bladder • fibrosis(radiation, TB), • Indwelling catheter • Anxiety	• Treat underlying cause • Reassess the indwelling catheter where applicable as mechanical irritation can be caused by the catheter balloon - change catheter/ reduce volume of the balloon • Catheter slugging with partial retention – bladder washouts or continuous • Bladder irrigation as described in the UTI section • Treat cystitis • Relieve obstruction/instability – especially related to catheter • Surgical intervention- tumor, Posterior Urethral Valve, Benign Prostatic Hyperplasia, stone. • Remove foreign body (catheter or stones) if obstructing bladder outlet • Treat Inflammatory causes • Institute non-pharmacological palliative interventions • Regular toileting • Appropriate fluid intake • Avoiding caffeine and alcohol • Prescribe appropriate first-line treatment • Treat bladder pain: WHO pain ladder • Add treatment for bladder spasms with: ○ Hyoscine Butylbromide 10-20 mg po, IV, IM or S/C tid. Maximum of 100mg per day – avoid if there is urinary retention ○ Consider adjuvant/second-line treatment ○ Intravesical morphine and bupivacaine tid (morphine 10-20mg and 0.5% bupivacaine 10ml diluted in 0.9% saline to 20 ml), instil through an indwelling catheter and clamp for 30 min. ○ Spinal analgesia, e.g. epidural morphine and 0,5% bupivacaine can be used if setup allows

23.3 SKIN CARE

ITCHING

- **Itching (pruritus):** is an irritation in the skin that elicits an urge to scratch.
- It is a problem that can be localized or generalized.
- Sometimes, it may be worse at night. A generalized itch and those without visible lesions are often more difficult to treat than a localized itch and those with visible skin lesions.
- Generalized itching with invisible lesion are usually due to systemic problems or allergies.

Causes	Management
• Infection :(Tinea Scabies, Sexually Transmitted Disease,HIV) • Contact with any skin irritants • Drugs(chemotherapy) • Neuropathies(DM, Herpes, MS) • Metabolic problems (renal failure, liver failure, hyperthyroid) • Dry skin • Sunburn • Insects • Psychological(Anxiety, Stress)	• General management options for itching o Avoid heat and hot water o Moisturise and hydrate dry skin o Apply calamine lotion o Menthol 1% in aqueous cream. o Zinc o To moisturize and hydrate the skin use aqueous cream as a soap substitute and bland bath oils o Apply an emollient (liquid paraffin, coconut oil) immediately after washing • Outpatient medication o Assess for infectious cause – if present, treat. o Consider and treat other underlying cause o If there are multiple skin infections, use a chlorhexidine (0.05%) rinse after bathing. o Consider that this may be the side-effects of medication. o Local steroid creams may be useful if inflammation is present in the absence of any infection- bacterial, fungal, or viral. • Anti-histamines o Cetrizine-10mg po once daily, Loratadine 10mg po daily (in children less than 30KG use 5mg po daily) o Chlorphenramine 4 mg twice daily, up to 4 mg every 4–6 hours (maximum 24 mg daily), or another antihistamine, may be useful for severe itching. o Diphenhydramine If the itching still persists, a short-acting antihistamine and a long-acting antihistamine (from different groups) could be combined for better symptom relief. • Home care for itching o If the affected person has dry skin, moisturize with aqueous cream or petroleum jelly mixed with water. • Avoid frequent bathing o Use 1 spoon of oil (bath or vegetable) in the bath water when washing. o Apply diluted Chlorhexidine (0.05%) after a bath, medicated soap

Pressure Sores

- **Pressure sores (decubitus ulcers)** are ulcers of the skin which can extend into the subcutaneous tissue caused by ischemia secondary to extrinsic pressure and shearing forces.

- **The most vulnerable areas** are elbows, shoulder blades, spine, buttocks and heels. If the patient is more comfortable lying on his/her side, then special attention should be given to ears, shoulders, hips and knees.

Causes	Management
• **Risk factors** ○ General debility ○ Neurological deficit ○ Reduced mobility ○ Coma ○ Incontinence ○ Cachexia ○ Dehydration ○ Anemia ○ Infection and poor hygiene ○ Others	• **Prevention of pressure sores** ○ Inspect the skin every time the patient is moved ○ The skin should be washed and dried regularly, including bed bath for bed ridden patient ○ Maintain suppleness of skin by regular massage with skin lotion ○ Avoid trauma – no restraints, lift patients do not drag them to move them in the bed ○ Regular positional change, family or hospice/hospital carers should assist in changing the patient's position every 2-4 hrs. depending on patient's risk factors ○ Keep the bed linen dry and free from creases ○ Keep the patient well-nourished and well hydrated ○ Using cushions to support joints helps the patient relax and prevent ligaments from being overstretched. ○ Special mattress (air or water mattress)to distribute body weight more evenly

WOUND CARE

- **General wound care:** in palliative care we mainly deal with chronic wounds.
- Chronic wounds are characterized by ischemia, lengthened inflammatory processes, increased protease concentration and reduced level of growth factor activity.

Causes	**Management**
• Classification o Mechanical (surgical and trauma) o Burns and chemical (thermal, radiological) o Chronic ulcerative wounds (pressure sores, leg ulcers, radiotherapy or malignancies) Post-operative o Factors that delay wound healing o Nutrition deficiency Anemia o Medications that slow wound healing-e.g. steroids, NSAIDs, Chemotherapy, Immunosuppressants o Other: Beta blockers, anticoagulants and phenytoin may delay healing. o Radiotherapy depletes dermal fibroblasts o locally and total body irradiation o Depresses bone marrow which causes minimizing of wound macrophages. o Drug and Alcohol abuse cause vascular injury and reduce the immune response o Ischemia and reduced blood supply (e.g. pressure) o Necrotizing malignancy • Location o Pressure sores commonly on heel, sacrum and Buttocks o Peripheral areas with poor local circulation o Position affects vascularity e.g. wounds over joint areas tend to heal slower. o Wound circumference and depth – ruler o Wound margins – redness could indicate infection, red/grey could be the result of undermining, white typifies maceration (excess moisture) • Exudate o Amount: A sudden increase may indicate infection but the presence of exudates is a necessary part of the healing process and varies during the different phases. o Appearance: serous, haemo serous,sanguineous, purulent o Odor: an offensive odor usually indicates the presence of high levels of bacteria. • Wound base o Dry and necrotic o Moist and sloughy o Granulating o Epithelializing	• Treat reversible factors o Wound specific treatment - Remove Necrotic Tissue - surgical – tweezers, scissors or a scalpel debridement as appropriate - Gauze soaked in adrenaline 1:1000 - Gentle removal of dressing with normal saline spray or irrigation using a syringe containing warm Normal Saline 0.9% to prevent trauma at dressing changes. • Infection o Irrigate wound with warm NS 0.9% or under running water. o Use antibiotics if there is spreading inflammation, not just a red rim. o Use appropriate antibiotics like Cloxacillin or Trimethoprim Sulfamethoxazole or Erythromycin o Choosing a dressing o Administer appropriate anti-pain during wound care o To maintain moisture o To add moisture o To absorb moisture o Protect wound surface o Control bacteria - Silver Sulphadiazine cream, Ichthammolglycerine, activated charcoal ± silver • dressings o Control odor - activated charcoal, see separate guidelines below

MALODOUROUS WOUNDS

- The wounds seen in palliative care patients are often a result of their advanced illness and/or poor physical or social state.
- Wound malodor can be a significant and distressing symptom for the patient, his/her family and care givers. Patients may experience embarrassment, disgust, guilt and shame, which can lead to social isolation and relationship problems.

MANAGEMENT

- **Correct reversible factors**

Malodor is often caused by anaerobic bacterial infection of the necrotic tissue within a fungating wound. Metronidazole has been shown to be effective.

- **Consider disease-specific treatment**

Treatment of lesions depends on the stage of the wound, size and the patient's general health:

Surgery (debulking) of large fungating tumors

  - Chemotherapy
  - Palliative radiotherapy
  - Hormone therapy for responsive tumors in breast cancer (Tamoxifen)

- **Non-pharmacological treatment of wound malodors**
  - Good hygiene:
    - Regular wound cleaning
    - Regular bedding and clothing changes
    - Adequate disposal of soiled dressings
    - Adequate ventilation
  - Dressings
    - Use highly absorbent dressings to contain a high level of exudate to control odor.

        - Preferably use non-adherent dressings (to make regular changing less painful)
    - Debridement
- **Pharmacological treatment of malodor in wounds**
    - Topical (For mildly infected wounds without cellulitis):
        - Metronidazole solution for cleaning a wound: 2liter saline + 10 (500mg) crushed metronidazole tablets to wash wound or area.
        - Metronidazole gel: KY jelly mixed with crushed metronidazole tablets applied to the wound
        - Metronidazole powder: crushed metronidazole tablets applied directly on to the wound
        - Metronidazole cream: aqueous cream mixed with crushed metronidazole tablets
        - Silver Sulphadiazine (Flamazine)
        - Bacitracin, Fucidin or antifungal ointments where appropriate
        - Charcoal dressings
        - Honey and yoghurt
    - Systemic: antibiotics for significant infections (preferably after obtaining a wound swab if possible)
        - Metronidazole 500mg tid/bid pediatric dosage PO until good effect is obtained. (Side-effects: nausea and alcohol intolerance).
        - Other antibiotics: Amoxicillin, Erythromycin, Trimethoprim Sulfamethoxazole .
        - Mono-therapy with Metronidazole is usually sufficient to address clostridial and bacteriods effects but sometimes staphylococcus and pseudomonas may colonize such wounds and need additional antibiotics such as Cloxacillin and/or Aminoglycosides
- Pain: Treat pain appropriately

23.4 INFECTION PREVENTION AND CONTROL

- Palliative care services shall operate in accordance with National Infection Prevention and Control Policy and standard guidelines to minimize the risk of infections in patients, families and care providers in order to promote a safe caring environment.
  - **Core infection prevention and control interventions shall include:**
    - Hand hygiene
    - Safe handling and disposal of patient excreta such as faeces, urine, sweat, and waste products
    - Use of personal protective equipment
    - Isolation precautions
    - Aseptic technique
    - Cleaning and disinfection and
    - Sterilization

23.5 NEUROPSYCHIATRIC SYMPTOMS AND THEIR TREATMENT

- Patients and their families/care givers shall be informed of common neuropsychiatric issues.
- A good assessment is key to support patients. Common neuropsychiatric symptoms in palliative care include anxiety, depression, insomnia and delirium. Each of these areas will be considered and their treatment discussed below.

Anxiety

- Anxiety is defined as a feeling of apprehension and fear characterized by physical symptoms such as palpitations, sweating, and feelings of stress.
- It is common in the terminally ill for a variety of reasons such as the fear of uncontrolled symptoms, fear of dying or being left alone to die.

Symptoms of Anxiety

- Core features: Persistently tense and unable to relax, worry, more than normal mood variation, cannot distract self.
- Symptoms: Poor concentration, indecisiveness, insomnia, irritability, sweating, tremor, nausea, panic attacks.
- **Assessment to identify cause and severity:**
    - Is it severe?
    - Is it long-standing?
    - Is it alcohol withdrawal?
    - Is it situational?
    - Is it related to a specific fear?
    - Are the family anxious?

Management:

- Correct reversible factors
- Non-pharmacological intervention: Psychological methods for managing anxiety. Psychotherapeutic Interventions

General treatment for most anxiety problems

- Psycho-education: this is the first and most important kind of treatment for all of mental health problems, helping people realize that their condition is common, treatable, and not something to be ashamed of.
    - These sorts of problems are very common
    - It is not a form of weakness – our bodies are designed to have these sorts of reactions

  - ○ Though most of these problems will not completely vanish, they almost always improve, though it can take time.

- Learning skills to reduce the effects of stress is the most effective relief.

- Help people become aware of when they are anxious and what seems to provoke it.

- This seems obvious, but, anxious behaviors can be a habit and not noticed.

  - ○ Trying to do things too fast or doing too many things at the same time
  - ○ Holding the body in a tense position, clenching fists, clenching jaw.
  - ○ For some people, impulsively eating
  - ○ When the patient is aware of being anxious or of cues to anxiety, try a method of relaxation:

- ▪ Take a few slow, deep breaths
- ▪ Have a motto or something to think about that reminds them to be calm
- ▪ Count slowly to 10 and then continue with whatever they were doing

- Try 'active coping'- if there is a feared issue or thing, try to work on dealing with it rather than avoiding (but all the while acknowledging that it's hard).

  - ○ For children (or even adults), reward brave behavior

Pharmacological Intervention

Drugs	Dosage	Description
Benzodiazepine		
Diazepam	2 to 5 mg p.r.n., p.o./ day	Diazepam has a long half-life and may therefore accumulate and be sedative. It should be possible to give it once a day, at night, although initially it can be given tds (three times a day).
Lorazepam	1 to 2 mg p.r.n., p.o. bid/day	Lorazepam is short-acting, rapidly anxiolytic and less sedating than diazepam. It may be more addictive on a longer-term basis.

Antidepressants		
Amitriptyline	25 to 50 mg po/day	
Imipramine	25 to 50 mg po/day	

Note: Refer if no response

DELIRIUM/ACUTE CONFUSION

- Delirium is an altered state of mind characterized by confusion of recent onset and variable severity.
- It is the most common and serious neuropsychiatric complication in the patient with advanced illness.
- It is a collective term for the various causes of acute confusion rather than a specific diagnosis.
- There are 4 key features of delirium that need to be present to make the diagnosis:
  - A changed level of consciousness (Difficulty focusing, sustaining attention, agitated, restless or drowsy. Disorientation).
  - A disturbance of the process of thinking/cognition (short term memory loss, disorganized thinking, speaking and problem solving, hallucinations and delusions).
  - The above changes are of recent onset and may fluctuate over a period of hours.
  - There is definite clinical evidence that the disturbance is caused by the abnormal physiology of an underlying general medical condition.
- There are 3 clinical sub-types of delirium;
  - **Hyperactive delirium**: The patient is restless, irritable, agitated and may become aggressive or inappropriate in their behavior.
  - **Hypoactive delirium**: The patient is inactive, disinterested and incoherent.

  - **Mixed delirium**:The patient fluctuates between hypo- and hyperactive delirium. This is the most common sub-type (>50%).

MANAGEMENT

- Correct reversible factors
- Consider disease-specific palliative therapy
  - Where appropriate rehydrate patients (orally or by infusion).
  - Review all medications, stop or reduce the dosage of all non-essential drugs and recheck for previous excessive alcohol or illicit drug use.
  - A trial of steroids for suspected brain metastases.
  - Most infections should be appropriately treated unless the patient has signs of impending death (within 24-48 hrs.).
  - Consider using bisphosphonates for hypercalcemia.

NON-PHARMACOLOGICAL INTERVENTIONS

- Calm reassurance of the delirious patient
- Regular orientation for time and place
- Presence of a family member- Limit visitors
- Identify and maintain care giver consistency were possible
- Familiar personal objects or photos
- Encourage walking, or if bedridden, range of motion exercises
- Appropriate lighting at night
- Soothing music
- Gentle back massage and a glass of warm milk rather than a sleeping tablet
- Noise reduction as far as possible
- Optimize vision and hearing (check hearing aid)

Note: Physical restraints are not necessary. They may aggravate the situation and cause injury. Effective calming and if necessary, sedation is possible by means of appropriate medication at effective dosages.

PHARMACOLOGICAL TREATMENT

Mild delirium without agitation			
Drug	Dose	Frequency	Comment
Haloperidol	0.5 - 2mg PO	Can be given every hour, for up to 3 doses and then should be reviewed. (Notify Dr if 3 doses not effective. This allows a review of the situation so that the dose can be adjusted if needed)	Usual effective dose is 0.5 -2mg/day Maintenance: Previous day's total used given as a single daily dose & the same p.r.n. dose for break though symptoms NB: Medication is not always needed but as agitation may occur unexpectedly in a new environment consider its use for a short period.

DELIRIUM WITH MILD AGITATION BUT NO AGGRESSION:			
Drug	Dose	Frequency	Comment
Haloperidol	1-2 mg IM	Can be given every hour, for up to 3 doses and then should be reviewed. (Notify Dr if 3 doses not effective.)	Usual effective dose is 6-12mg/day Maximum 20mg/day Maintenance: Previous day's total used given as a single or divided dose plus the same p.r.n. dose for break though symptoms

DELIRIUM WITH AGITATION, RESTLESSNESS AND AGGRESSION:

Drug	Dose	Frequency	Comment
Haloperidol	3-5mg, SC, IM or IV	Can be given every hour, for up to 3 doses and then should be reviewed (Notify Dr if 3 doses not effective.)	Up to 20 mg IM per day. Occasionally prolongation of the Q-T interval may occur. An aggressive delirious patient may be dangerous and calming the patient must be an urgent priority for all staff. (See second line drugs)

Alternative first line drug:

Drug	Dose	Frequency	Comment
Chlorpromazine	12.5 – 50 mg PO, IM or	Every 2-4 hours p.r.n. x3 (Notify Dr if 3 doses not effective.)	More sedating than haloperidol. May cause hypotension, measure BP

Note: Delirium presents many complex clinical and ethical problems. If the degree of uncertainty about the diagnosis and management is interfering with proper care, consult the advice of a more experienced specialists (Psychiatrists and psychiatric nurses).

Insomnia

- Insomnia is the inability to fall asleep or to remain asleep for an adequate length of time. Insomnia is present when all three of the following criteria are met:
  - A complaint of difficulty initiating sleep, difficulty maintaining sleep, and waking up too early.
  - The above sleep difficulty occurs despite adequate opportunity and circumstances for sleep.
  - The impaired sleep produces deficits in day time functions

ASSESSMENT TO IDENTIFY CAUSE AND SEVERITY OF SYMPTOMS

- It is important to get a thorough history of the patient's sleep pattern now and before he/she started to have problems.
- Establish the patient's understands about insomnia and their expectations.
- Identify possible medications that the patient is taking that could be causing the insomnia.
- Identify possible emotional stresses that could be causing the insomnia.
- Identify possible symptoms such as pain that may be causing the insomnia

MANAGEMENT

- Correct reversible factors
    - Identify and treat the primary condition; e.g. pain
    - Eliminate disturbance and noise
- Consider disease-specific palliative therapy
    - Treat insomnia with a holistic approach
    - Consider physical, psychosocial and spiritual causes and management options
- Institute non-pharmacological interventions
    - Avoid alcohol and stimulants in the evening
    - Relaxation techniques
    - Massage
    - Warm milk/herbal tea at night
    - Cognitive-behavioral therapy
    - Progressive muscle relaxation therapy
    - Hypnotherapy

- Sleep hygiene
- Substitute radio or relaxed reading
- Avoid large meal near bed time

PHARMACOLOGIC MANAGEMENT

- Benzodiazepines have been successfully used for short term insomnia, although there are no systematic studies on long-term use and rare studies in palliative care.
  - Diazepam 5 to 10 mg at night
  - Lorazepam 1- 2 mg at night
  - Bromazepam 1.5 to 3 mg PO at night
  - Amitriptyline can also be used to treat short term insomnia.

DEPRESSION

- Depressed mood and sadness may be an appropriate response to approaching death for the terminally ill patient.
- It is often under diagnosed and under-treated. It is important to identify depression as conventional treatment achieves a good response in the majority of patients.
- If untreated, depression can result in worsening of symptoms and in social withdrawal and even suicide.

CLINICAL FEATURES

- Depressed mood
- Loss of interest or pleasure in almost all activities
- Anorexia
- Marked weight loss or gain
- Insomnia / hypersomnia / early morning awakening
- Loss of self esteem

- Feelings of worthlessness / helplessness / guilt
- Poor concentration / indecision
- Thoughts of death or suicide

COMMON CAUSES

- Uncontrolled pain or other symptoms
- Loss of independence
- Lack of support from family / friends / healthcare workers
- Fear – of dying or death
- Drugs – steroids, diazepam, efavirenz
- Loss of body image, due to disfigurement

MANAGEMENT

- Relieve pain and other distressing symptoms
- Review / modify drug treatment
- Provide counseling, support, reassurance
- Drugs – Treatment of depression can significantly improve quality of life and is as effective in palliative care as in other situations.
  - ***Tricyclics***
    - Amitriptyline 25-75 mg at night
    - Imipramine 25-75 mg per day, if available, is an alternative that might be less sedating
  - ***Selective serotonin re-uptake inhibitors (SSRIs)***
    - Fluoxetine 20 to 40 mg in the morning (morning with meal)
    - Sertraline 50 to 100 mg per day (morning after meal with meal)

Note: Consult psychiatrist if there is no improvement.

  - 'Start low, go slow'
  - Antidepressants should not be stopped abruptly if at all possible, but withdrawn gradually.

SUICIDE IDEATION

CLINICAL FEATURES

- The frequency of suicide in the cancer population is higher than in the general population with the highest risk in the months after diagnosis.
- The risk decreases with survival time and is low in the terminal phase.
- Depression is a factor in at least 50% of all suicides.
- Treatment of depression can diminish desire for death.
- Feelings of hopelessness – loss of purpose in living – may be associated with suicide intent independently of depression.
- Completed suicide is rare in cancer patients.
- Suicidal thoughts are common in terminally ill patients but are usually fleeting & are often associated with feelings of loss of control & anxiety about the future.
- The desire to hasten death in not necessarily synonymous with a request to hasten death.

ASSESSMENT OF PATIENTS WHO MAY BE AT RISK OF SUICIDE

- Depression is common in the general community and more so in patients with advanced illness. Separating the clinically depressed patient from the person overwhelmed or despairing of their illness and circumstances may not be easy.
- Questions that can help assessment:

4. 'Are you depressed?'
5. 'Recently have you often been bothered by feeling down, depressed or hopeless?'

6. 'During the last month have you often been bothered by little interest or pleasure or doing things?'
7. 'Have you felt things getting too much for you?'
8. 'Have you been scared you might harm yourself?'
9. 'Do you feel you have lost purpose for your life?'

- The above have been shown to be reliable indicators of patients who may need further exploration of their depressive symptoms and possible treatment.
- It is also important to reassure patients that many people in their circumstances feel this way at times but these thoughts are often fleeting and diminish with time.

Management

- Treat underlying depression
- For a patient who has persistent suicidal thoughts in the absence of an underlying depression, intervention and support from mental health services may be advisable.

23.6 PSYCHOSOCIAL AND SPIRITUAL CARE AND SUPPORT

SOCIAL CARE AND SUPPORT IN PALLIATIVE CARE

- Social care is an important part of the inter-disciplinary team within palliative care, offering holistic service to patients and families.
- Social care is potentially a universal service and supports clients facing long-term situations involving life-limiting illness, dying, death, grief, and bereavement.
- Using the expertise of social workers with populations from varying cultures, ages and socio-economic status social workers help patients & families across the life span in coping with trauma, suicide, and death.

- Social work practice addressing palliative and end of life care include; hospitals, hospices, home care, nursing homes, child welfare, civil society's organizations, faith based organizations and family service agencies.
- Social work to chronically sick people deals with a range of problems associated with patients and of his/her family.
- These include: stigma and discrimination, isolation, economic crisis, housing, daily living, dependency for physical needs, cultural influences, religion, psychosocial issues and orphan care.

SPIRITUAL CARE

- Spiritual care involves being a compassionate presence to patients even as they suffer. It recognizes that emotional and spiritual healing can take place even though a physical cure is impossible.
- As a patient approaches end of life they often begin to think about the meaning and purpose of life and feel the need to mend broken relationships by forgiving and being forgiven.
- Areas of life that can generate spiritual peace or spiritual distress are relationship with God/Creator/Higher Being, with self, with others, and with the world around them.
- Spirituality can be defined completely by the individual's culture.
- Spirituality can also be individually defined by personal experiences unrelated to the culture.

WHY IS SPIRITUALITY IMPORTANT?

- Physical healing and psychological coping may be complicated if patients are experiencing spiritual distress.
- Appropriately addressing patients' spiritual concerns and needs can contribute to more rapid recovery and better prognosis.
- Spirituality can bring an ill person hope, strength, and emotional support

ROLE OF COMMUNICATION IN PALLIATIVE CARE

- The foundation of palliative care is built on good communication with patients, family members and health care professionals.

- People living with a life-threatening illness often have many concerns about their care and feel isolated.
- The palliative care professional needs to spend time to discuss the patient's problems which may include psychosocial and spiritual problems as well as their physical symptoms.
- When discussing a patient's diagnosis or prognosis the palliative care professional needs to be able to communicate effectively with the patient and family.
- This may take some time and requires a step-by-step approach. The palliative care professional needs to assess the patient and family's desire to know about the life-threatening illness and ensure that the patient and family receive and understand the information as they request and is culturally appropriate.

CARE OF THE CARE GIVERS

- Caring for people with a life-threatening illness is a complex process.
- Family carers support the patient physically, psychologically, spiritually and economically.
- Palliative care supports the family as they care for their loved one.
- It is important that the health care professionals assess the needs of the carers as well as the patient and should assess the carers for burnout or exhaustion and provide support as necessary.
- Working with palliative care patients is time consuming and can be emotionally exhausting. So, it is important that health care professionals have regular support meetings with other colleagues and are offered psychological support as required.
- Self-care is imperative when working in palliative care.
- Heath care professionals should ensure that:

4. Are able to prioritize activities

5. Accept that you can only change things within your control and cannot alleviate all suffering
6. Tell superiors when you feel overloaded
7. Set yourself realistic/achievable goals
8. Monitor your workload
9. Take leave regularly (short breaks during the year and one long break annually)
10. Do not continuously work excessive hours of overtime
11. Are not exposed to any unnecessary risks
12. Monitor your own health and well-being.

23.7 END OF LIFE CARE

- End of life care is about the total care of a person with an advanced incurable illness and does not just equate with dying.
- The end-of-life care phase may last for weeks or months.
- End of life care provides physical, mental and emotional comfort, as well as social support, to people who are living with and dying of advanced illness.
- Health care providers shall prepare both the patient and the family on the impending death:
  - Care provider shall be honest, attend to emotional responses and spiritual needs.
  - Care providers shall maintain presence and talking to the patient even if he/she is unconscious.
  - Comfort measures shall be provided depending on the presenting signs and symptoms of impending death.
  - End-of-life concerns, hopes, fears, and expectations shall be openly and honestly addressed in the context of social and cultural customs in developmentally appropriate manner.

- Palliative care practice shall be guided by the medical-ethical principles of autonomy, beneficence, non-maleficence and justice.

Care Suggestions for the Family When Death is Imminent

Changes	**Care Suggested**
Decreased social interaction	• Encourage the family to remain in the same room and not leave the patient alone, explaining the calming effect of a human presence.
Decreased consciousness	• Encourage the family to talk to and touch the patient. • Skin care and pressure relief become crucial at this point.
Increased discomfort, general aches and pains of being bedridden	• Continue analgesics even if the patient is comatose or can no longer swallow. Use alternative routes of administration if appropriate. • Reduce the dose if there is an increased risk of side effects (such as myoclonic jerks) which may be treated with any benzodiazepine.
Reduced interest in and intake of food and drink	• Explain the natural physiological process to the family. • Discourage force feeding and allow family to offer sips of water or chips of ice hourly to keep the mouth moist. • If the family requests for intravenous fluids in any setting (hospital, clinics, home), explain the consequences.
Decreased urinary and GIT output	• Reassure the family that the patient is not uncomfortable. • Address possible incontinence and the need for extra careful skin care. • Repeat information about measures to protect the care giver against body fluids.

Changes in breathing (irregular, stopping and starting, or noisy–the 'death rattle')	• Explain what is happening and reassure the family. • Keep the mouth moist, especially if the patient is mouth breathing. • Consider using hyoscine butyl bromide by various routes to reduce secretions.
Changes in circulation (cold and grey or blue/purple hands, feet, nose and ears)	• Explain that death is near. • Encourage the family to stay with the patient.
If the patient faces social or financial problems	Link with appropriate stake holders

EUTHANASIA

- **Euthanasia** means the deliberate 'killing' of a human being to relieve their suffering or to relieve him/her of life in a body judged to be unable to function normally by others.
- In Ethiopia, patients may express severe pain in terms of voicing the wish to 'die than suffer'.
- It is however important to note that the primary request of patients is actually to be relieved from pain and suffering not a wish to die.
- This is often in conflict with their family's pleas to hang on at all costs and their religious conviction that when and how to die should be left to a

higher power, but also addressing the immediate suffering of such patients through appropriate management.

- Euthanasia is condemned according to Ethiopia law.

BEREAVEMENT ISSUES AT THE END OF LIFE

- Bereavement is the period of adjustment in which the bereaved learns to live with the loss.
- Grief is the normal, dynamic process that occurs in response to any type of loss. It encompasses physical, emotional, cognitive, spiritual, and social responses to the loss.
- Anticipatory grief begins as soon as a loved one develops symptoms perceived as life-threatening.
- Mourning is the public expression of grief. This public expression (perhaps crying or wailing) does not necessarily relate to the significance of the loss; it is usually related to cultural and religious values and encourages social support for the mourner.
- Complicated mourning arises from an interrupted or obstructed grief process, and can result in potentially harmful outcomes, from somatic discomfort to chronic emotional distress, and even the possibility of death.

GRIEF COUNSELLING

- Most support after a death will be/ should be provided by family and friends.
- Grief counselling is used to help survivor adapt.
- A brief contact at time of loss, more extended contact 1 to 2 weeks after funeral

WHAT TO DO NEAR TIME OF DEATH?

- Patient and Family need assistance in handling their anticipatory grief in ways that enable them to take care of themselves and their loved one:
    - Helping to address practical issues, such as food, accommodation, and care for their children

  - Identifying and legitimizing feelings of sadness, anger, guilt, and anxiety
  - Encouraging expression of feelings in privacy
  - Enabling them to complete unfinished business
  - Encouraging family to live fully and enjoy life whenever and wherever they can
  - As people face their death, they want to know they will be remembered and that their life has had meaning.
  - Using religious rituals
  - Tradition in Ethiopia requires close family gather around the bedside of the dying person.
  - Any important 'last words' will be said
  - Sensitivity and courteous respect of a dying patient is crucial, with attention to the patient's family's needs. These last moments will be remembered in great detail.
  - Remark on comfort of patient so family is informed and reassured

AFTER DEATH:

- Allow time with body
- Practicalities: remove implanted devices, complete death certificate, inform other clinicians
- Acknowledge the loss: share memories of the deceased, give permission to grieve, and do not take sides in family disputes.
- Networking with other resources and organizations: health care professionals should be networked with community and faith-based organizations that can assist bereaved individuals, families, or child-headed households.
- Visiting the bereaved/family: The bereaved appreciate gestures and expressions of condolence and sympathy, including telephone calls, and visits

- Encourage community involvement using existing community based structures like ‘ iddir’
- Encouraging good self-care. Encourage appropriate physical exercise, proper diet, and rest, other spiritual activities if they have.

GRIEF THERAPY

- Grief Therapy seeks to identify and resolve conflicts that have caused some degree of ‘complicated grief’.
- For example: chronic grief, delayed grief, exaggerated grief or the response and the presence of persisting somatic pain and other symptoms of distress.
- Patients with complicated grief are best treated by psychiatrists or clinical psychologists

FURTHER READING:

1. Ethiopian National Palliative care guideline, 2016

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